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Running head: TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

CONTRASTING TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR PATIENTS
WITH HEAD AND NECK CANCER TREATED WITH RADIOTHERAPY WITH OR WITHOUT
ADJUNCTIVE CHEMOTHERAPY

By

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Dissertation

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immense impression on me and gave me a desire to become a leading expert in the area of swallowing disorders. That desire eventually led me to the path of a Ph.D.

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Table of Terms and Abbreviations

ASHA	American Speech-Language-Hearing Association
Aspiration	When food or liquid enters the airway below the level of the glottis
BMI	Body Mass Index
CRT	Chemoradiation therapy
C-PSE	Prophylactic swallowing exercises consisting of direct and indirect exercises
DNA	Deoxyribonucleic acid
EAT	Eating Assessment Tool
Enteral nutrition	Nutrition delivered via a feeding tube
EORTC QLQ-C30	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
FACT-H&N	Functional Assessment of Cancer Therapy-Head and Neck
FEES	Fiberoptic endoscopic evaluation of swallowing
FOIS	Functional Oral Intake Scale
HADS	Hospital Anxiety and Depression Scale
HIPAA	Health Insurance Portability and Accountability Act
HNC	Head and neck cancer
HNSCC	Head and neck squamous cell carcinoma
HPV	Human papilloma virus
HRQOL	Health related quality of life
ID-PSE	Prophylactic swallowing exercises consisting solely of indirect swallowing exercises
IRB	Institutional Review Board
MASA	Mann Assessment of Swallowing Ability
MBS	Modified barium swallow study
MDADI	M.D. Anderson Dysphagia Inventory
MRI	Magnetic Resonance Imaging
PAS	Penetration-Aspiration Scale
PSE	Prophylactic swallowing exercises
PEG	Percutaneous Endoscopic Gastronomy
PSS-H&N	Performance Status Scale for Head & Neck Cancer
QOL	Quality of Life
QLQ-H&N35	Quality of Life Questionnaire-Head and Neck Cancer Module
RT	Radiation Therapy
SLP	Speech Language Pathologist
TNM	Tumor Node Metastasis

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Abstract

Slovarp, Laurie, Ph.D., Summer 2015

Independent Interdisciplinary Studies

Contrasting Two Prophylactic-Dysphagia Interventions for Patients with Head and Neck Cancer Treated with Radiotherapy with or without Adjunctive Chemotherapy

Co-Chairperson: Catherine Off, Ph.D., CCC-SLP

Co-Chairperson: Julie Liss, Ph.D.

Many patients with head and neck cancer (HNC) suffer from dysphagia caused by organ preserving regimens of radiation therapy with or without adjunctive chemotherapy. Prior research has shown a benefit of prophylactic dysphagia intervention; however, prior studies vary in terms of timing, dosage, and types of treatments prescribed. Additionally, compliance to prophylactic swallowing exercises (PSEs) has been poor and anecdotal evidence points towards swallowing pain as a cause of poor compliance. This prospective study investigated exercise compliance, oral intake, self-perceived swallowing function, swallowing-related quality of life, and swallowing-related pain for patients who received two different types of prophylactic swallowing interventions. A total of 18 participants partook of the study. Nine patients completed only indirect swallowing exercises (exercises that do not require swallowing; ID-PSE group). The remaining nine patients completed a combination of indirect and direct swallowing exercises (exercises that require swallowing; C-PSE group). There were no significant differences between the groups at baseline or at any point during RT/CRT. The ID-PSE group performed significantly better than the C-PSE group at one month post-RT/CRT in swallowing function, as measured by the Eating Assessment Tool, and swallowing-related QOL, as measured by the MD Anderson Dysphagia Inventory. By three months post RT/CRT these differences were not present; however, at three months post the C-PSE group reported significantly less swallowing pain than the ID-PSE group. Between-group differences were not evident at any point in compliance or oral intake. Outcomes for both groups were comparable to prior PSE studies and better than outcomes reported in the literature in HNC patients who did not receive prophylactic intervention. This study is the first to investigate and provide preliminary evidence for the efficacy of a prophylactic swallowing intervention consisting solely of indirect swallowing exercises. Study limitations, clinical implications, and future directions are discussed.

Key words: dysphagia, prophylactic swallowing exercises, head and neck cancer, radiotherapy, chemoradiation therapy, quality of life, pain, swallowing function

Chapter 1: Introduction

Head and neck cancer (HNC) refers to malignant tumors of the oral cavity, pharynx, or larynx. It is the eighth most common cancer among men and 14th most common among women in the United States (Chaturvedi, Engels, Anderson, & Gillison, 2008). HNC is estimated to impact nearly 600,000 patients per year and over 300,000 deaths (Marur, D'Souza, Westra, & Forastiere, 2010). The most common histological type of HNC is squamous cell carcinoma, which arises in the mucosal lining of the mouth, pharynx, or larynx. Patients are usually diagnosed between 40 and 55 years of age. A significant increase in the rate of HNC, specifically in the oropharynx (tonsil and tongue base area), has been documented in recent years (Marur et al., 2010).

For decades, tobacco and alcohol use were the primary causes of HNC; however, approximately 40% to 80% of oropharyngeal cancers in the United States are now associated with the human papillomavirus (HPV; Marur et al., 2010; Sudhoff et al., 2011). In fact, non-smokers who are HPV positive are now 15 times more likely to develop HNC than smokers (Sudhoff et al., 2011). Numerous types of HPV exist; however, the vast majority (>90%) of HPV-associated HNCs is caused by a single type--HPV 16 (Marur et al., 2010; Sudhoff et al., 2011). While the incidence of head and neck cancer secondary to smoking has fallen steadily since the 1970s, HPV-associated HNC has been increasing steadily (Auluck et al., 2010; Marur et al., 2010; Sudhoff et al., 2011). One study estimated that if recent incident trends continue, the annual number of HPV-associated oropharyngeal cancer will surpass the annual number of cervical cancer by 2020 (Chaturvedi et al., 2011). The most current studies of medical care costs for HPV-related oropharyngeal cancer estimate a cost of \$306 million per year for the United States (Chesson et al., 2012) and \$519 million per year for France (Borget, Abramowitz, & Mathevet, 2011).

Fortunately, significant advances of the treatment of HNC have emerged in the past two

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decades. Prior to the 1990s, the standard treatment for HNC was surgical dissection (with or without adjunctive radiation therapy), or radiation therapy (i.e., radiotherapy or RT) alone (Forastiere et al., 2003a). This practice changed in the early 1990s when the Department of Veteran Affairs Laryngeal Cancer Study Group showed that chemotherapy followed by RT was as effective as the traditional approach of surgery plus radiation (Department of Veteran Affairs Laryngeal Cancer Study Group, 1991). Subsequent research determined that RT given concurrently with chemotherapy (ChT), commonly referred to as chemoradiation therapy (CRT), is more effective than chemotherapy followed by RT (Forastiere, Koch, Trotti, & Sidransky, 2001; Forastiere et al., 2003a; Milas, Mason, Liao, & Ang, 2003).

CRT has since emerged as the standard of care for HNC and is described as the best course of treatment for organ preservation (Forastiere et al., 2003a; Milas et al., 2003; Samant et al., 1999). The term “organ perseveration,” however, is arguably a misnomer since it does not necessarily mean that persevered organs have preserved function. The organs may be preserved anatomically, but the toxic effects of RT/CRT severely damage any tissues within the radiation field. Consequently, organs treated with RT/CRT rarely function normally again (Jensen, Lambertsen, & Grau, 2007; Rieger, Zalmanowitz, & Wolfaardt, 2006).

Swallowing impairment (dysphagia) is one example of impaired organ function resulting from RT/CRT toxicity. Dysphagia is the most common side effect of RT/CRT and is recognized as one of the most devastating consequences of treatment (Greven et al., 2008; McColloch, Carroll, & Magnuson, 2010). Dysphagia secondary to RT/CRT toxicity can occur during treatment (acute), last for several months following RT/CRT (chronic), and can return years after initial symptom resolution (late; Goguen et al., 2006; Gurney, Eisele, Orloff, & Wang, 2008; Hutcheson et al., 2008; K. Jensen et al., 2007; Koiwai, Shikama, Sasaki, Shinoda, & Kadoya, 2010; Kotz, Costello, Li, & Posner, 2004;

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Shiley, Hargunani, Skoner, Holland, & Wax, 2006). Radiotherapy and chemotherapy given in isolation contribute to their own toxic side effects. Those side effects are compounded when radiation and chemotherapy are given concurrently, because chemotherapy intensifies the effects of radiation (Forastiere et al., 2001). RT/CRT toxicities include but are not limited to: inflammation, reduced taste, xerostomia (dry mouth), oral mucositis (painful inflammation and ulceration of the mucosal lining in the oral and pharyngeal cavities), tissue fibrosis (scar tissue), and dental cavities (Agarwala & Sbeitan, 2006; Gaziano, 2002; Groher & Crary, 2010).

Severe dysphagia caused by RT/CRT toxicity frequently leads to the need for enteral nutrition (Cheng et al., 2006; Ishiki et al., 2012; J. Lee et al., 1998). In fact, enteral nutrition is so common among patients treated with RT/CRT for HNC that many physicians now recommend feeding-tube placement prophylactically before beginning RT/CRT (Ishiki et al., 2012; J. Lee et al., 1998; Maurer, Hipp, Schafer, & Kolbl, 2011). Over 50% of patients remain dependent on a feeding tube at five months post RT/CRT (Greven et al., 2008; Ishiki et al., 2012), and 10% to 30% continue to be dependent at one year post (Ishiki et al., 2012; Paleri & Patterson, 2010). Some patients never regain functional swallowing ability and end up feeding-tube dependent for the remainder of their lives (Hutcheson & Lewin, 2012; Maurer et al., 2011; Newman et al., 1998).

Although most patients eventually regain oral intake sufficient to meet their nutritional needs and remove their feeding tubes, few regain fully normal swallowing function. Up to 82% of patients continue to have some level of functional deficit in swallowing at 12 months post-treatment (List et al., 1999) and less than 50% are able to resume a normal diet (Garcie-Peris et al., 2007; Logemann et al., 2008). Common symptoms include difficulty eating dry foods, food sticking in the mouth or throat, and coughing on food or liquid secondary to penetration or aspiration (i.e., when food or liquid enters the airway). As a result of these deficits, many patients have to alter their diets, eat and drink with

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caution, and/or use compensatory swallowing strategies, all of which contribute to reduced quality of life (Harrison et al., 1997; Hutcheson et al., 2008; List et al., 1997; Maurer et al., 2011; Nguyen et al., 2006).

Speech-language pathologists (SLPs) play a primary role in assessing and treating patients with dysphagia as a result of to HNC (Lazarus, 2000; Murphy & Gilbert, 2009; Paleri et al., 2014; Roe et al., 2012). The SLP's job is to assess the patient's swallowing function, and determine the necessity and course of treatment. Ideally a thorough assessment should follow the World Health Organization (WHO) model and include assessment of activity limitations and participation restrictions as a result of the swallowing impairment (World Health Organization, 2013). The goal of therapy is to improve or maintain efficient and safe oral nutritional intake, minimize the risk of aspiration pneumonia, and optimize quality of life.

Historically, SLPs did not take an active role in managing dysphagia in patients with HNC until the patient completed cancer treatment (McColloch et al., 2010). In the 1990s, it became more common for SLPs to see patients prior to or during RT/CRT, with the primary purpose of educating the patient about side effects related to swallowing and monitoring their swallowing function (Lazarus, 2000; Logemann, Pauloski, Rademaker, & Colangelo, 1997; McColloch et al., 2010; Patterson & Wilson, 2011; Pauloski et al., 2000; Roe & Ashforth, 2011). Recent research, however, has shown a benefit of active prophylactic swallowing intervention prior to and during cancer treatment to minimize dysphagia (Carnaby-Mann, Crary, Schmalfuss, & Amdur, 2011; Carroll et al., 2008; Kulbersh, 2006; van der Molen et al., 2011; Virani, Kunduk, Fink, & McWhorter, 2015). Although these studies have shown promising results, significant methodological differences and a lack of standardized procedures preclude any valid comparisons across studies. Further, most of the studies report poor compliance to the exercise programs (Carnaby-Mann et al., 2011; Kotz et al., 2012; Virani et al., 2015).

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Statement of the Problem

The majority of patients with HNC treated with RT or CRT experience debilitating dysphagia, which is, in part, a direct result of the cancer treatment. Prophylactic swallowing exercises (PSE) have been shown to improve functional swallowing outcomes; however, current available studies vary widely in treatment protocol and outcome measures (McColloch et al., 2010; Roe & Ashforth, 2011). Hence, a uniform best-practice protocol has not been established. Additionally, prior PSE studies report poor compliance to PSE programs (Carnaby-Mann et al., 2011; Kotz et al., 2012; van der Molen et al., 2011; Virani et al., 2015) and anecdotal evidence suggests that swallowing pain is a main contributor to poor compliance (Kotz, Abraham, Beitler, Wadle, & Smith, 1999). Although current available data is encouraging, many unanswered questions remain regarding the most effective and essential exercises, the most ideal treatment schedule and intensity, the relationship of patient variables to specificity of treatment (e.g., tumor location, tumor size, cancer stage, age), and how best to maximize patient compliance and QOL.

Purpose

The purpose of this study was to provide further insight into the best way to treat patients diagnosed with HNC suffering from dysphagia secondary to CRT toxicity. This study specifically sought to determine if a PSE program consisting solely of indirect swallowing exercises (exercises that do not require actual swallowing; ID-PSE) is more effective and more acceptable to patients than a PSE program consisting of a combination of direct (exercises that require swallowing) and indirect swallowing exercises (C-PSE). Previous PSE studies have included a combination of direct and indirect swallowing exercises. Yet, each of the previous PSE studies that mention compliance, report poor compliance (Carnaby-Mann et al., 2011; Kotz et al., 2012; van der Molen et al., 2011; Virani et al., 2015). We hypothesized that swallowing pain is the primary reason for poor compliance and that

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swallowing pain is worsened when doing direct swallowing exercises. Based on this hypothesis, we also hypothesized that indirect swallowing exercises would be more comfortable for patients and, consequently, would result in improved compliance to PSE exercises. Improved compliance would, in turn, result in better swallowing function outcomes. The following research questions and hypotheses guided this study.

Research Questions and Hypotheses:

1. In patients undergoing RT/CRT for HNC of the tongue, palate, pharynx, or larynx, is there a difference in compliance between patients treated with ID-PSE and similar patients treated with C-PSE?
 - a. Null hypothesis: There will be no difference in the compliance dependent variable between patients completing ID-PSE and patients completing C-PSE.
 - b. Alternative hypothesis: Patients completing ID-PSE will report higher percentages on the exercise compliance dependent variable than patients completing C-PSE.
2. Are oral intake outcomes different between patients undergoing RT/CRT for HNC treated with ID-PSE and similar patients treated with C-PSE?
 - a. Null hypothesis: There will be no significant difference in the oral intake dependent variable (percent oral intake, FOIS, PEG-tube dependency) between the ID-PSE and C-PSE groups.
 - b. Alternative hypothesis: The ID-PSE group will report greater scores on the oral intake dependent variable, as measured by percent oral intake, FOIS, and PEG-discontinuation rate, than the C-PSE group.
3. Are swallowing function outcomes different between patients undergoing RT/CRT for HNC completing ID-PSE and similar patients completing C-PSE?

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Null hypothesis: The swallowing function dependent variable outcomes, as measured by the EAT-20 and the MDADI, will not differ between patients treated with ID-PSE and patients treated with C-PSE.

Alternative hypothesis: The ID-PSE group will report better scores on the swallowing function dependent variable, as measured by the EAT-20 and MDADI, than patients treated with C-PSE.

4. Does a difference exist for the level of swallowing pain between patients completing ID-PSE and patients completing C-PSE?

Null hypothesis: Patients treated with ID-PSE will not report different levels of the swallowing pain dependent variable than patients treated with C-PSE.

Alternative hypothesis: Patients treated with ID-PSE will report lower scores on the swallowing pain dependent variable, as measured by a 0-5 scale, than patients treated with C-PSE.

Chapter 2: Literature Review

Human papilloma virus (HPV) is now the primary cause of oropharyngeal head and neck squamous cell carcinoma (HNC; Auluck et al., 2010). It has contributed to an exponential increase in incidence of HNC as well as a reduction in the average age at diagnosis (Chaturvedi et al., 2008). Fortunately, advances in radiotherapy (RT) and chemoradiotherapy (CRT) have contributed to improved survival rates and a reduced need for radical surgical dissection (Department of Veteran Affairs Laryngeal Cancer Study Group, 1991; Forastiere et al., 2003b). Radiotherapy and CRT, however, comes with significant negative side effects on swallowing function and quality of life (e.g., swallowing pain, dry mouth, impaired swallowing function, and reduced participation due to impaired swallowing function (Langmore & Krisciunas, 2010; Lazarus et al., 2000; Logemann et al., 2008). Recent research has focused on understanding the pathophysiological impacts on swallowing due to RT/CRT toxicity, how to minimize these impairments, and how best to maximize quality of life.

Swallowing Function

Normal swallowing is a highly coordinated and complex process that involves over 30 muscles and six cranial nerves (Groher & Crary, 2010; Logemann, 1998). Swallowing occurs in four phases: oral preparatory, oral, pharyngeal, and esophageal. During the oral preparatory phase the bolus (i.e., food or liquid being swallowed) is prepared for swallowing. During the oral phase the bolus is transported from the oral cavity into the pharynx. The pharyngeal phase begins as the bolus passes the ramus of the mandible on its way to the pharynx, at which point the pharyngeal swallow response is initiated and is driven by muscular contraction and pressure. Negative pressure develops below the bolus as the entrance to the esophagus opens, while contraction of the pharyngeal constrictor muscles and the base of the tongue provide positive pressure above the bolus to drive the bolus downward. Simultaneously, the laryngeal valve closes, protecting the airway from aspiration. When the food

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passes through the upper esophageal sphincter (UES), the esophageal phase begins. This phase is also pressure driven and highly coordinated. The esophageal muscles superior to the bolus contract in a sequential motion while the esophagus below the bolus relaxes, allowing the bolus to be propelled inferiorly.

Dysphagia

Dysphagia is the term used to describe an impairment of swallowing. Dysphagia can involve one or more of the four phases of swallowing described above and the nomenclature used to describe dysphagia parallels the swallowing phases (Logemann, 1998). Oral dysphagia describes dysphagia isolated to impairment during the oral preparatory or oral phases. Pharyngeal dysphagia is specific to impairment during the pharyngeal phase. Esophageal dysphagia describes dysphagia during the esophageal phase. Dysphagia most commonly involves both the oral and pharyngeal phases and is termed oropharyngeal dysphagia. Common symptoms of oropharyngeal dysphagia include delayed or prolonged mastication time, delayed or poorly coordinated transport of the bolus from the oral cavity into the pharynx, delayed initiation of the pharyngeal swallow response, reduced clearance of food or liquid through the oral or pharyngeal cavities, impaired airway closure resulting in food or liquid entering the airway above the vocal folds (i.e., penetration) or below the vocal folds (i.e., aspiration), and impaired opening of the UES.

Interdisciplinary Approach to Dysphagia Management

Dysphagia is managed by a number of healthcare professionals. Physicians manage the medical aspects of the disorder, which may include surgical intervention, treatment for aspiration-related pneumonia, and pharmacological intervention for things such as pain management, treatment of oral infections, and treatment for a variety of esophageal disorders (e.g., gastroesophageal reflux, esophageal spasms) ((Groher & Crary, 2010; Murry & Carrau, 2006). If a patient has difficulty

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swallowing efficiently, or cannot swallow safely and requires enteral nutrition, it is the job of the dietitian to make appropriate diet recommendations in order for the patient to meet his/her nutritional needs (Groher & Crary, 2010; Logemann, 1998). Dietitians and physicians work closely with speech-language pathologists (SLPs), whose role is to assess oropharyngeal swallowing function, make recommendations related to swallowing safety, and provide behavioral treatment as appropriate. Behavioral treatment, consisting of diet modifications, swallowing exercises, and/or swallowing strategies, is the most common form of management of oropharyngeal dysphagia (Groher & Crary, 2010; Logemann, 1998; Murry & Carrau, 2006).

Swallowing Assessment

Three primary assessment tools are used to assess oropharyngeal swallowing function: clinical (or bedside) swallowing evaluation, modified barium swallow study (MBS), and fiberoptic endoscopic evaluation of swallowing (FEES; Groher & Crary, 2010; Logemann, 1997). A clinical swallow evaluation includes a detailed case history of subjective complaints, current and past medical status and treatment, an oral mechanism examination, and physical examination during swallowing trials. The purpose of the clinical swallow evaluation is to determine the patient's ability to prepare and move the bolus from the oral cavity to the pharynx, assess coordination of swallow response timing, subjectively assess hyolaryngeal elevation and excursion with palpation, and look for signs or symptoms of aspiration (Gaziano, 2002; Lazarus, 2000; Patterson & Wilson, 2011). The clinical swallow evaluation is a valuable assessment tool but is limited in that it cannot objectively determine the presence and severity of aspiration, the amount and location of pharyngeal residue, or the exact physiological impairment contributing to these symptoms (Groher & Crary, 2010). A MBS or FEES, which provide video imaging of the swallow in real time, is often necessary because of these limitations.

A modified barium swallow (MBS) study is a radiological examination performed under

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videofluoroscopy in a radiology suite (Logemann, 1997). Videofluoroscopy allows visualization of the oral, pharyngeal, and upper esophageal phases of swallowing while the patient ingests food and liquid mixed with barium. An SLP directs the exam, typically with the assistance of a radiologist. The SLP administers various consistencies of food and liquid to the patient while observing the patient's swallowing function under fluoroscopy (i.e., continuous x-ray imaging). The SLP assesses safety and tolerance of each type of texture and trials compensatory swallowing strategies as appropriate, if the patient presents with a functional swallowing impairment.

A fiberoptic endoscopic evaluation of swallowing (FEES) is an endoscopic exam whereby a flexible fiberoptic endoscope is passed transnasally to the level of the soft palate for a superior view of the pharynx and larynx while the patient ingests food and liquid. Reliability studies comparing FEES to MBS have shown FEES to be a reliable measure in regards to pharyngeal and laryngeal function (Colodny, 2002; Leder, Sasaki, & Burrell, 1998; Schatz, Langmore, & Olson, 1991); however, a FEES does not allow visualization of the oral cavity or esophagus, which is a significant disadvantage in the case of head and neck cancer patients who often present with deficits in these areas (Pauloski, 2008). For this reason, MBS is the more commonly used instrumental exam. The goal of either exam is to determine whether or not a patient is safe for per oral (P.O.) nutrition, the exact nature of the swallowing impairment, the safest and least restrictive diet for the patient, the usefulness of swallowing compensatory strategies, and what physiological impairments should be targeted in treatment (Agarwal et al., 2011; Bleier et al., 2007; Lazarus, 2000; Logemann, 1997; Patterson & Wilson, 2011; Pauloski, 2008).

Swallowing Treatment

Behavioral treatment options for oropharyngeal dysphagia fall into two broad categories -- compensatory swallowing strategies (i.e., postural modifications, bolus size and consistency

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modifications, swallowing maneuvers) and restorative swallowing exercises (i.e., active exercises to improve range of motion (ROM), coordination, and/or strength of oral, pharyngeal, or laryngeal structures) (Pauloski, 2008; Robbins et al., 2008). Compensatory strategies improve swallowing function while the strategies are performed but do not result in long-term physiological improvement; hence, the patient only benefits from compensatory strategies when he/she is actively using the strategies (Loeb, Becker, Eady, & Walker-Dilks, 2003; Pauloski, 2008). Restorative therapy, on the other hand, is intended to improve swallowing physiology to minimize or eliminate swallowing impairment (Pauloski, 2008; Robbins et al., 2008).

Restorative therapy is most appropriate for prophylactic intervention for patients with HNC treated with RT/CRT because of its goal to minimize physiological impairment. The primary overarching pathophysiological cause of dysphagia in patients with HNC treated with RT/CRT is reduced range of motion secondary to edema and tissue fibrosis (Tang et al., 2011) and muscle weakness, secondary to disuse atrophy (Langmore & Krisciunas, 2010). Restorative therapy in these patients should, therefore, target range of motion and strengthening of swallowing structures.

Range of motion (ROM) exercises. Range of motion exercises for the jaw, tongue, and larynx are designed to stretch and move the structures in all directions in order to improve or maintain ROM and flexibility, which is necessary for functional swallowing as well as speech. While research has not clearly defined an optimal exercise schedule and intensity, five to 10 repetitions of each exercise per session and a goal of five to 10 sessions per day is generally recommended (Logemann, 1998; Pauloski, 2008). Logeman et al. (1997) provided pilot data showing that HNC patients who completed jaw, tongue, and laryngeal ROM exercises following RT exhibited significantly better speech and swallowing function than those who did not complete ROM exercises.

Jaw ROM exercises. Restricted jaw opening as a result of radiation fibrosis following RT or

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CRT is termed *trismus*. Current treatment options for jaw ROM include passive stretch exercises such as finger-assisted mouth opening, stacked tongue depressors, and use of the Therabite device (a device inserted in the mouth that passively stretches the mouth aperture by the patient squeezing a lever) (Buchbinder, Currivan, Kaplan, & Urken, 1993; Dijkstra, Sterken, Pater, Spijkervet, & Roodenburg, 2007; Tang et al., 2011). The patient may also actively stretch by simply opening the mouth as wide as possible and holding the stretch for two seconds. The patient is also instructed to move the jaw side to side in the same fashion (Logemann et al., 1997; Tang et al., 2011). Several studies have shown the benefits of these exercises for relieving trismus (Buchbinder et al., 1993; Cohen, Deschler, Walsh, & Hayden, 2005; Tang et al., 2011).

Tongue ROM exercises. Tongue ROM can also be limited due to the effects of radiation fibrosis following RT or CRT. Tongue ROM exercises are done actively. The patient is instructed to move the tongue forward and back, side to side, and in a circle (Logemann et al., 1997). Elevation of the back of the tongue can be targeted by the patient placing the tongue in the position for producing the /k/ or /g/ sound. This stretch can be increased by the patient holding the tongue in the /k/ position and then opening the jaw as far as possible (Logemann, 1998).

Laryngeal ROM exercises. Laryngeal elevation and excursion (upward and forward movement of the laryngeal complex) is important for airway closure and epiglottic inversion, both of which are important for moving the bolus through the pharynx, without residue left behind and without aspiration (Logemann, 1998). Reduced laryngeal elevation/excursion is correlated with limited oral intake and diet in HNC patients within the first year following treatment (Pauloski et al., 2006). Three exercises are designed to target laryngeal elevation and excursion, including effortful pitch glide, Mendelsohn maneuver, and the Shaker exercise.

Effortful pitch glide. The effortful pitch glide, also termed the *pharyngeal squeeze* (Fuller,

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Leonard, Aminpour, & Belafsky, 2009) and *falsetto voice* (Pauloski, 2008), involves gliding the voice up the pitch scale and then sustaining a high-pitched voice as long as possible. The rationale for the exercise is that during high-pitched voice production the larynx elevates and the pharyngeal constrictors contract to a similar extent as during swallowing (Fuller et al., 2009; Miloro, Langmore, & Pearson Jr, 2014).

Mendelsohn maneuver. The Mendelsohn maneuver is an intentional prolongation of laryngeal elevation at the height of the swallow. The maneuver has been shown to improve the extent of laryngeal elevation as well as upper esophageal sphincter opening, both of which are commonly impaired in HNC patients treated with RT or CRT (Kahrilas, Logemann, Krugler, & Flanagan, 1991; Lazarus, Logemann, & Gibbons, 1993).

The Shaker exercise. The shaker exercise is an isometric/isokinetic exercise designed to improve UES opening and laryngeal elevation by contracting the suprahyoid muscles responsible for laryngeal elevation/excursion (Shaker et al., 1997). Since both laryngeal elevation/excursion and reduced UES opening are common following RT/CRT for HNC, there is a strong rationale for using this exercise with this population.

The Shaker exercise is done with the patient in a supine position. During the isometric portion of the exercise, the patient lifts the head so that the chin approaches the chest. This position is held for one minute, followed by a one-minute rest. During the isokinetic portion of the exercise, the patient lifts and lowers the head 30 times, with a hold time of only two to three seconds at the top. Strong evidence exists for the efficacy of this exercise for improving anterior laryngeal movement and UES opening (Easterling, Grande, Kern, Sears, & Shaker, 2005; Shaker et al., 2002).

Oral and pharyngeal strengthening exercises. Reduced strength of the tongue and pharyngeal constrictors is well documented in patients with HNC treated with RT/CRT (Eisbruch et

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al., 2002; Kotz et al., 1999; Kotz et al., 2004; Smith, Kotz, Beitler, & Wadler, 2000). The following exercises are commonly prescribed for improving tongue and pharyngeal constrictor strength.

General tongue strengthening. Tongue strength is typically targeted by pressing the tongue against a wooden tongue depressor, or something similar, to provide resistance. The tongue can be pressed straight out, to the right and left, and up and down. Lateral tongue strength also can be targeted by pressing the tongue against each cheek (Logemann, 1998). Tongue resistance exercises have been shown to be effective in healthy individuals as well as stroke patients (Clark, O'Brien, Calleja, & Corrie, 2009; Robbins et al., 2005; Robbins et al., 2007), but to date only one study has been published on tongue strengthening exercises in patients with HNC treated with RT/CRT (Lazarus et al., 2014). Lazarus and colleagues compared tongue-strengthening exercises paired with traditional swallowing exercise to traditional swallowing exercises alone in patients post-RT/CRT treatment for HNC. They found no statistically significant differences between the two groups on measures of tongue strength or swallowing function. The authors postulated that poor compliance to the program may have contributed to the findings.

Tongue base retraction strengthening. Tongue-base retraction refers to movement of the posterior tongue towards the posterior pharyngeal wall. Tongue base retraction is essential during swallowing to assist in pressing food or liquid through the pharynx into the esophagus (Logemann, 1998). Impaired tongue-base retraction is one of the most common physiological impairments following RT/CRT for HNC (Eisbruch et al., 2002; Lazarus, 2000; Lazarus et al., 2007). Common exercises for strengthening tongue-base retraction include: repetitive pulling of the tongue as far back as possible into the oral cavity (i.e., the tongue pull-back; (Veis, Logemann, & Colangelo, 2000), gargling (Johnson, Herring, & Daniels, 2014; Veis et al., 2000), yawning (Johnson et al., 2014; Veis et al., 2000), the effortful swallow (Hind, Nicosia, Roecker, Carnes, & Robbins, 2001; Huckabee, Butler,

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Barclay, & Jit, 2005; Huckabee & Steele, 2006; Lazarus et al., 1993; Pouderoux & Kahrilas, 1995), and the Masako maneuver (Fujiu & Logemann, 1996). The gargle task has proven to be more effective than the tongue pull-back and pretending to yawn (Veis et al., 2000). The effortful swallow and Masako are described separately below.

The effortful swallow. The effortful swallow is a strengthening exercise whereby the patient squeezes all of the muscles used for swallowing as strongly as possible during the swallow. The patient is instructed to pay attention to pushing the tongue up against the palate (Huckabee & Steele, 2006). The effortful swallow is often prescribed as a compensatory strategy as it has been shown to reduce pharyngeal residue after the swallow by improving movement of the bolus through the pharynx (Hind et al., 2001; Huckabee et al., 2005; Huckabee & Steele, 2006). Biomechanically, the effortful swallow results in increased oral and pharyngeal pressure, prolonged laryngeal closure, increased hyolaryngeal elevation and excursion, and prolonged distention of the UES (Hind et al., 2001; Hiss & Huckabee, 2005; Lever et al., 2007). In this regard, the effortful swallow can be prescribed for improving tongue-base retraction, hyolaryngeal elevation and excursion, pharyngeal contraction, and UES opening. A number of studies have shown the effortful swallow to be effective in HNC patients treated with RT/CRT (Carnaby-Mann & Crary, 2010; Crary, Carnaby, LaGorio, & Carvajal, 2012; Lazarus, Logemann, Wook Song, Rademaker, & Kahrilas, 2002).

The Masako maneuver. The Masako, or tongue-hold, maneuver is performed by swallowing while the tongue is anchored between the front teeth. This exercise has been shown to improve tongue-base retraction and pharyngeal contraction (Fujiu & Logemann, 1996). Lazarus and colleagues (2002) provided evidence that this exercise improved pressure and duration of contact between the tongue-base and posterior pharyngeal wall during the swallow in patients with HNC treated with RT.

Numerous restorative swallowing exercises have been designed and validated to improve

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swallowing physiology. However, designing the most appropriate prophylactic swallowing exercise protocol specifically for patients with HNC treated with RT or CRT requires an understanding of RT/CRT and the associated toxicity that contributes to dysphagia.

The Interaction between Radiation Therapy and Chemotherapy

To understand how RT/CRT toxicity impact swallowing function, it is helpful to review how RT works and how chemotherapy (ChT) interacts with RT during CRT. There are two forms of RT – external beam and internal. External beam radiation is delivered from outside the body by aiming a beam(s) of radiation to the location of the cancer, while internal radiation is delivered internally by placing radioactive sources directly into a cancer site (Baskar, Lee, Yeo, & Yeoh, 2012). External beam radiation is the most common approach used to treat HNC (Baskar et al., 2012). Regardless of the delivery method, radiation therapy works primarily by damaging the DNA of cells, thereby reducing their ability to divide and proliferate (Baskar et al., 2012).

Multiple complex cellular mechanisms are involved during radiation-induced cellular DNA damage, but two common types of damage are single-strand breaks and double strand breaks (Seiwert, Salama, & Vokes, 2007a). Double strand breaks (DSBs) involve breaking of both strands of the DNA double helix. This type of break is irreparable and leads to certain cellular death; however, DSBs are not easily achieved. Single strand breaks (SSBs), on the other hand, involve just one strand of the DNA double helix. SSBs are relatively easy to achieve, but they are not likely to lead to cellular death because the breaks are easily repaired through cellular repair mechanisms (Baskar et al., 2012; Seiwert et al., 2007a). It is, in part, because of these repair mechanisms that chemotherapy added adjunctively to RT (as in CRT) is more effective than non-synchronous RT and chemotherapy. Chemotherapy (ChT) drugs are believed to interfere with damaged cells' ability to repair themselves, thereby increasing the rate of cell death. In this way, ChT is said to act as a radio-sensitizing agent (Baskar et

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al., 2012; Seiwert et al., 2007a; G. Wilson, Bentzen, & Harari, 2006).

The most common ChT drug given to patients with HNC during CRT is Cisplatin (Seiwert et al., 2007a; Seiwert, Salama, & Vokes, 2007b). In addition to Cisplatin interfering with cellular repair mechanisms to increase cellular death following RT-induced DNA damage, Cisplatin also interacts with nucleophilic sites on DNA and RNA, which distorts the DNA structure and interferes with nucleotide replication and transcription (Seiwert et al., 2007b).

Unfortunately, the cellular damage caused by RT/CRT effects normal cells as well as cancer cells. The primary outcome goal of RT/CRT, therefore, is to: (1) maximize radiation and cellular death in cancer cells, while (2) minimizing radiation exposure and cellular death in normal cells. Delivering RT in fractions and advances in delivery and imaging techniques have helped improve these outcomes.

Fractionation. Radiation therapy is generally delivered in fractions, which consists of several small doses of radiation rather than less frequent larger doses (Baskar et al., 2012). The purpose of a fractionated RT schedule is to enhance the survival of normal cells over cancer cells. This is explained by the differences in radiobiological properties of cancer cells and normal cells. Normal cells tend to divide and proliferate more slowly than cancer cells; whereas, cancer cells tend to divide and proliferate rapidly. By delivering RT in smaller, sublethal doses, normal cells have a chance to repair themselves before replicating. However, cancer cells are likely to replicate themselves before DNA damage has been repaired (Baskar et al., 2012). The typical RT schedule for patients with HNC is 35 fractions of 1.8 to 2 Gy of radiation per fraction, delivered five days per week (Mallick & Waldron, 2009).

Intensity modulated radiation therapy. Intensity modulated radiation therapy (IMRT) is the current standard radiation delivery method for patients with HNC (Lee & Terezakis, 2008). IMRT is an advanced method of delivering radiation three-dimensionally using multiple radiation beams to

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maximize radiation dose to the intended target with a sharp radiation gradient at the planned margin to minimize the dose to normal tissue. The radiation oncologist uses imaging studies to outline the target area. This information, as well as the desired radiation dose, is analyzed by a computer-optimized algorithm, which determines the most likely treatment plan that maximizes radiation to the target area, while minimizing radiation to the surrounding normal tissue. IMRT has been shown to reduce xerostomia and preserve other anatomical structures relative to traditional RT (Eisbruch, 2005).

Image-guided radiotherapy. As treatment margins have increasingly tightened to spare normal adjacent tissue, so has the necessity to increase accuracy of each RT dose. Image-guided radiotherapy (IGRT) has been born out of this necessity (Baskar et al., 2012). Tightening treatment margins comes with an increased risk of missing cancerous tissue at or near the margin of the radiation field. Additionally, slight positional errors from one RT session to the next may result in missing small portions of cancerous tissue in one area while increasing unintentional exposure to critical structures in another area. IGRT uses pre-radiation imaging to detect and correct for such errors before each RT session. Head and neck and prostate tumors are two common sites that benefit from IGRT (Baskar et al., 2012).

Despite these advances, patients with HNC treated with RT or CRT continue to suffer from significant negative side effects due to RT/CRT toxicity. These side effects contribute to dysphagia in nearly all patients during treatment and up to 64% of patients post-treatment (Francis, Weymuller, Parvathaneni, Merati, & Yueh, 2010; Hutcheson & Lewin, 2012).

RT/CRT Toxicity-Induced Dysphagia

Mucositis, xerostomia, and reduced taste are the most common acute side effects caused by RT/CRT toxicity that impact swallowing. Mucositis results in inflammation and ulceration of the mucosal lining in the oral and pharyngeal cavities and contributes to severe oral and throat pain

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(Rodriguez-Caballero et al., 2011). This pain contributes to severe odynophagia (i.e., painful swallowing). Mucositis typically begins within two to three weeks of the onset of RT/CRT, gets progressively worse throughout, and then gradually declines over a matter of weeks to months following completion of RT/CRT. It is not uncommon for the pain to become significant enough to require narcotic analgesics (e.g., morphine; Agarwala & Sbeitan, 2006; Elting et al., 2008). Xerostomia typically begins within a few weeks of beginning RT/CRT and also gets progressively worse (de Castro Jr. & Honda Federico, 2006). Dry mouth contributes to thick saliva that, for many patients, causes gagging. Xerostomia improves somewhat following RT/CRT but a majority of patients suffer to some extent from chronic dry mouth for the rest of their lives (Braam et al., 2005; Büntzel, Glatzel, Mücke, Micke, & Bruns, 2007; de Castro Jr. & Honda Federico, 2006; S. B. Jensen et al., 2010). Reduced taste also begins during RT/CRT and usually resolves within several months following completion of treatment (Vissink, Jansma, Spijkervet, Burlage, & Coppes, 2003). Mucositis, xerostomia, and reduced taste cumulatively result in avoidance of oral feeding (some patients avoid swallowing all together) at some point during RT/CRT. Lack of swallowing then contributes to disuse atrophy of the swallowing muscles (Franzmann, Lundy, Abitbol, & Goodwin, 2006), which further contributes to dysphagia. These side effects resolve significantly within a few weeks following the last RT/CRT (Elting et al., 2008); however, return of normal and safe swallowing function takes much longer as a result of the time required for the swallowing muscles to regain functional strength (Frowen & Perry, 2006).

The primary late side effect of RT/CRT that contributes to dysphagia is radiation-induced fibrosis (Delanian & Lefaix, 2007; O'Sullivan & Levin, 2003; Stubblefield, 2011). Fibrosis is scar tissue of the connective tissue that was exposed to radiation and is less common than mucositis and xerostomia. In simplistic terms, it is caused by dysregulation of aspects of wound healing including

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up-regulation of transforming growth factor β 1, a peptide involved in collagen production (Bleier et al., 2007; Delanian & Lefaix, 2004). Fibrosis contributes to hardening of connective tissue, which impacts flexibility and range of motion, which is essential for functional swallowing. Fibrosis is generally considered irreversible, but some studies have shown improvements with antioxidant therapy, anti-inflammatory treatment, and vascular treatment (Delanian & Lefaix, 2004; Delanian & Lefaix, 2007).

RT/CRT toxicities cumulatively contribute to the following biomechanical and pathophysiological impairments that contribute to dysphagia: reduced tongue-base retraction, reduced tongue control, delayed swallow initiation timing, weak pharyngeal contraction, reduced epiglottic inversion, reduced laryngeal excursion, poor closure of the laryngeal vestibule, and reduced or shortened opening of the UES (Chang et al., 2003; Frowen & Perry, 2006; Hutcheson et al., 2008; Kotz et al., 2004; Logemann et al., 2008; Smith et al., 2000). These impairments contribute to difficulty transporting food from the mouth to the pharynx, premature spillage of food into the pharynx, difficulty getting food through the pharynx into the esophagus, and aspiration that is often silent (Hutcheson & Lewin, 2012; Nguyen et al., 2009; Nguyen et al., 2006).

The grueling nature of RT/CRT therapy also has a significant negative impact on QOL (de Graeff et al., 1999; El-Deiry, Futran, McDowell, Weymuller Jr, & Yueh, 2009; List et al., 1997; Ringash et al., 2008; Rogers, Ahad, & Murphy, 2007) and studies show unequivocally that swallowing function is directly correlated with QOL (Garcie-Peris et al., 2007; Hammerlid, Silander, Hörnestam, & Sullivan, 2001; Harrison et al., 1997; Maurer et al., 2011; Oates et al., 2007). This is not surprising given the strong cultural emphasis on eating and drinking at social gatherings. This association speaks to the importance of following the World Health Organization (WHO) model, which dictates consideration of activity limitations and participation restrictions when creating the most optimal prophylactic swallowing intervention protocol (World Health Organization, 2013).

Quality of Life During and Following RT/CRT for HNC

A vast literature base exists on QOL in patients with HNC. Rogers et al.(2007) conducted a structured review and theme analysis of papers on QOL over a 10-year span and found a total of 165 papers with a range of 18 to 34 publications per year. Over 50 QOL instruments were used across the papers, the majority of them validated. The sheer vastness of papers and QOL instruments designed specifically for patients with HNC attests to the importance of the topic. This review will highlight some of the most common instruments used to assess QOL in patients with HNC, including the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30 (EORTC QLQ-C30) and the EORTC QLQ-Head and Neck Cancer module (QLQ-H&N35), the Performance Status Scale for Head and Neck Cancer Patients (PSS-HN), the Functional Assessment of Cancer Therapy-Head and Neck (FACT-H&N), and the MD Anderson Dysphagia Inventory (MDADI).

The EORTC QLQ-C30 is in its 3rd version. It is a patient-based survey instrument for assessing health-related QOL of cancer patients, and consists of a global scale as well as five functional subscales: physical, role, emotional, cognitive, and social. The EORTC QLQ-Head and Neck Cancer module (QLQ-H&N35) is a supplementary module specific to head and neck cancer. This module consists of six symptom scales (pain, swallowing, taste/smell, speech, social eating, and social contacts) and seven single items (sexuality, teeth problems, problems opening mouth, dry mouth, sticky saliva, cough, and feeling ill). Both the EORTC QLQ-C30 and the QLQ-H&N35 modules have been vetted for validity and reliability specific to the HNC patient population. Reliability scores range from .72 to .87 and construct validity correlations are in the acceptable range with other valid instruments (Arraras et al., 2002; Bjordal & Kaasa, 1992; Bjordal et al., 1999; Bjordal et al., 2000; Chie, Hong, Lai, Ting, & Hsu, 2003; Osoba, Aaronson, Zee, Sprangers, & Velde, 1997).

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The PSS-HN is a clinician-rated QOL instrument with three subscales: normalcy of diet, understandability of speech, and eating in public. Each subscale is scored from 0 to 100 with better performance indicated by higher scores. Original validation data indicated reliability scores of .84 for Normalcy of Diet, .43 for Understandability of Speech, and .81 for Eating in Public. The scale was found to have sufficient validity for discriminating HNC from other types of cancer (List et al., 1996; List, Ritter-Sterr, & Lansky, 1990).

The MDADI, developed by Chen and colleagues (2001), is a self-administered, Likert-scale questionnaire designed and validated specifically for evaluating the impact of dysphagia on QOL in patients treated for HNC. This measure consists of 20 items and includes global, emotional, functional, and physical subscales. Each question is scored from 1 to 5 with 5 indicating the best QOL. The mean of each subscale is multiplied by 20 to obtain a score between 0 (extremely low functioning) and 100 (high functioning). Original validation and reliability research was completed by Chen et al.(2001) who validated the MDADI against the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) on 100 HNC patients. Reliability coefficients for the MDADI subscales ranged from .85 to .93. Test-retest reliability of the subscales ranged from .69 to .88.

The FACT-H&N was originally developed by Dr. David Cella and colleagues in 1993 and is now in its 4th version (Webster, Cella, & Yost, 2003). It is a self-report instrument that consists of a core questionnaire called the FACT-G, and a disease-specific subscale for HNC patients. The FACT-G consists of 28 general QOL items and HNC subscale consists of 11 QOL items. Each item is rated on a 0 to 4 Likert-type scale with a higher score indicating better QOL. Items are combined to indicate functioning in six areas: physical well-being, social and family well-being, relationship with doctor, emotional well-being, functional well-being, and head and neck related symptoms. The FACT-H&N has been tested mainly as a discriminative measure. It has met the minimum acceptable reliability

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requirements ($>.70$; List et al., 1996) and construct validity has been demonstrated in two studies (D'Antonio, Zimmerman, Cella, & Long, 1996; List et al., 1997).

Maurer (2011) used the EORTC QLQ-C30 and the EORTC H&N 35 to assess QOL before treatment, end of treatment, and six and 12 months post-treatment in 35 patients with HNSCC treated with RT or CRT. At the beginning of therapy, dysphagia caused by surgery or the tumor itself did not influence global QOL scores. However, at the end of treatment, the severity of dysphagia was highly correlated with a decline in global QOL score ($p = .03$, $r = -.321$). This correlation was maintained at six and 12 months post-treatment.

One of the largest QOL studies on this population was conducted by Hammerlid et al. (2001). They followed 232 patients with HNC. Over 90% of the patients were treated with RT or CRT. The patients were followed throughout treatment and for three years following treatment. QOL was measured with the EORTC QLQ-30 and QLQ H&N35. All but two of the single item scores deteriorated significantly between baseline and three months after treatment onset. The largest changes were found for senses, dry mouth, role function, loss of appetite, fatigue, overall pain, pain specific to oral and pharyngeal structures, swallowing, and social eating. At six months, all QOL domain and single item scores had improved except for problems with dry mouth and teeth. At a three-year follow-up, 13 of the single item scores had deteriorated further with the largest deteriorations in dry mouth, senses, and teeth. A logistic regression analysis indicated that in regards to emotional functioning, pain was the only predictor of global QOL and emotional functioning and swallowing pain predicted the degree of pain.

List et al.(1999) used the Functional Assessment of Cancer Therapy-Head and Neck (FACT-H&N) and the Performance Status Scale for Head and Neck Cancer Patients (PSS-HN) to assess QOL in 64 HNC patients treated with CRT at baseline, acutely (towards the end of CRT), and at three-month

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intervals following CRT. During the acute phase, a substantial decline was observed across most areas of QOL with the most significant decreases in *global performance status* and *normalcy of diet* on the PSS-HN, and *physical, functional*, and *overall well-being* on the FACT-H&N. Post-treatment data showed a gradual improvement in QOL, with many, but not all, subscales reaching baseline status. The most common complaints at 12 months post CRT were swallowing, hoarseness, and mouth pain.

Wilson (2011) used the MD Anderson Dysphagia Inventory (MDADI) to assess QOL on 167 HNC patients treated with CRT. They administered the MDADI before treatment and at three, six, and 12 months after treatment. On average, QOL scores declined by 18% from baseline to three months post-treatment and there was minimal improvement in QOL scores for the group as a whole between three months and 12 months post-treatment. The strongest predictor of QOL scores at 12 months was total radiation dose, with patients receiving 50 Gy or less having the best outcomes.

In summary, an extensive literature base demonstrates chronically reduced QOL in patients treated for HNC and dysphagia is a primary contributor to reduced QOL. Additionally, Hammerlid et al. (2001) found that swallowing pain was a predictor of global QOL. Any dysphagia intervention model for patients suffering from RT/CRT-toxicity-induced dysphagia should, therefore, consider QOL, specifically swallowing-related pain.

Treatment Models for Management of RT/CRT-Toxicity-Induced Dysphagia

The Reactive Model. The traditional model for dysphagia management in patients with HNC treated with RT/CRT is reactive in nature. In this model patients are referred for swallowing treatment only if his/her dysphagia does not resolve after a recovery period following RT/CRT (McColloch et al., 2010). The primary criticism of this model is that these patients do not receive adequate education and counseling regarding swallowing-related side effects during RT/CRT, the likely rehabilitation needs following RT/CRT due to dysphagia, and they are given minimal education in dysphagia symptoms to

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watch for or how to compensate for those symptoms. Patients' understanding of what is to come and their responsibility in the recovery process enhances the prognosis for ultimate successful rehabilitation (Logemann et al., 1997). Consequently, an educational/monitoring model has emerged that involves a much earlier referral to speech-language pathology.

The Educational/Monitoring Model. In the 1990s many physicians began adhering to an educational/monitoring model. This model dictates referral to an SLP prior to RT/CRT treatment with the purpose of obtaining baseline swallowing function, educating the patient about swallowing-related side-effects of RT/CRT, and monitoring swallowing safety throughout treatment to maximize safety of nutritional intake and to determine if and when the patient needs a feeding tube (Lazarus, 2000; Logemann et al., 1997; McColloch et al., 2010; Patterson & Wilson, 2011; Pauloski et al., 2000; Roe et al., 2012). Although this model is favored over the reactive model (Logemann et al., 1997; Patterson & Wilson, 2011) it is still a passive approach to dysphagia management and does nothing to minimize or prevent RT/CRT-induced dysphagia. Inherently, a model that prevents or minimizes dysphagia would be superior to both the reactive and educational/monitoring models.

The Prophylactic Model. Recent research has revealed the benefits of a proactive intervention model that employs active swallowing exercises prior to and during RT/CRT with the goal of minimizing RT/CRT-induced dysphagia. To date, seven published studies have demonstrated a benefit of prophylactic swallowing exercises (PSE) in patients with HNC treated with RT or CRT (Ahlberg et al., 2011; Carnaby-Mann et al., 2011; Carroll et al., 2008; Kotz et al., 2012; Kulbersh, 2006; van der Molen et al., 2011; Virani et al., 2015) and one study has shown no benefit of prophylactic intervention (Ahlberg et al., 2011). Overall, research shows promise towards validating prophylactic intervention; however, relatively few studies have been completed and those that have been completed vary markedly in methodology and do not include effect sizes, preventing cross-study comparison.

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Additionally, compliance to PSE programs has been poor; yet, only one PSE study considered compliance when designing the PSE program (Virani et al., 2015). A summary of each of the prior PSE studies can be viewed in Table 1.

Carroll et al. (2008) conducted the first randomized control trial investigating prophylactic dysphagia intervention for patients with HNC treated with RT or CRT. Eighteen participants treated with CRT for HNC were included in the study. Nine control participants received reactive swallowing therapy following CRT (if needed) and nine experimental participants received prophylactic swallowing exercises (PSE) that began two weeks prior to CRT. The exercises included tongue resistance, Masako, effortful swallow, Mendelsohn maneuver, and Shaker exercise. All exercises were performed with 10 repetitions, five times per day except the Shaker, which consisted of three, one-minute holds, and 30 repetitions (the authors did not specify how many times per day the Shaker was prescribed). Outcome measures for the study included a modified barium swallow study (MBS) three months post-CRT. The MBS measured hyoid movement, tongue-base retraction, epiglottic inversion, opening of the upper esophageal sphincter, and the penetration-aspiration scale (PAS; validated by Rosenbek, Robbins, Roecker, Coyle, & Wood, 1996). Significant differences were found between the two groups in tongue-base retraction and epiglottic inversion. Specifically, the experimental group had better tongue-base retraction and epiglottic inversion than the control group; in fact, six of the nine patients in the control group had no epiglottic inversion, whereas only one patient in the exercise group had no inversion. The groups did not differ in regards to PEG tube removal time, which the researchers suspected was a result of sample size.

The primary weaknesses of Carroll et al. (2008) include the following: (1) none of the measurements used indicated functional deficits in swallowing; (2) outcome measures were only taken at three months post-CRT, which may have missed differences that occurred earlier or later in the post-

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CRT phase, (3) they did not include a measure of QOL, and (4) they did not report on compliance to the PSE program.

Kotz et al. (2012) also conducted a randomized controlled trial comparing a PSE program to a reactive dysphagia intervention program. The experimental group ($n = 13$) received PSE that began at the beginning of RT/CRT and continued through RT/CRT. The control group ($n = 13$) was offered dysphagia treatment if the patient had dysphagia symptoms after completion of RT/CRT. All but one patient was treated with CRT for a newly diagnosed HNC. One patient was treated with RT alone. Patients were excluded if surgery was a part of their cancer treatment, if they had a tracheostomy, if they had undergone previous RT, or if they had a neurologic disease that could impact swallowing function. Prophylactic exercises consisted of: effortful swallow, Masako, tongue base retraction, the super-supraglottic swallow technique, and the Mendelsohn maneuver. The patients were instructed to complete three sets of 10 repetitions of each exercise daily and to vary the order of the exercises. Assessments included the Performance Status Scale for Head and Neck Cancer patients (PSS-H&N) and the Functional Oral Intake Scale (FOIS), as well as PEG removal time post-RT/CRT (for patients who required a PEG). The participants were assessed at baseline, within one week of the completion of RT/CRT, and at three months, six months, nine months, and 12 months post-RT/CRT. Results of the PSS-H&N and FOIS followed similar patterns; no significant differences between the groups existed at treatment-end, or at nine months or 12 months post-CRT. The experimental group was significantly better than the control group at three months and six months post-CRT for both the PSS-H&N and the FOIS, indicating a faster recovery in the experimental group. Twelve of the patients required PEG tubes. PEG-removal time was on average three months post-CRT and there was no significant difference between the two groups ($p = .15$), which is not surprising given the small group sizes. Kotz et al. also reported that 69% of the intervention patients were unable to continue the

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exercises throughout the entire course of CRT. Approximately half of the participants quit the exercises after four weeks and the other half quit after five weeks.

Several strengths and weaknesses of Kotz et al. (2012) inform the current study. The data collection schedule Kotz et al. used adequately captured group differences within one year of RT/CRT. Significant differences were found at three and six months post RT/CRT but not before or after three and six months, indicating that the most optimal time to capture short-term differences is within the first six months post RT/CRT. The primary weakness of Kotz et al.'s PSE program was the poor compliance to the program. Kotz et al. reported that poor compliance was not specifically due to an effect of the prophylactic exercises, but was rather due to oral and throat pain as well as general fatigue. However, given that four out of the five exercises required swallowing, which would likely exacerbate oral and throat pain, it is reasonable to suspect that poor compliance was related to the exercises causing pain. A more comfortable PSE program may have resulted in improved compliance and subsequent improved outcomes.

Kulbersh (2006) used similar prophylactic exercises as Carroll et al. (2008) and Kotz et al. (2012) but compared two different initiation timings of PSE. He used a prospective cohort design comparing the effectiveness of PSE initiated two weeks prior to the onset of RT or CRT (pre-treatment; n=25) to PSE beginning the first day of RT or CRT (concurrent-treatment; n=12). The Mendelsohn maneuver, Shaker, Masako maneuver (tongue-hold), tongue-resistance, and falsetto phonation¹ were prescribed for both groups. All exercises except the Shaker were prescribed for 10 repetitions, five times per day. The isometric Shaker was prescribed three times per day and the isokinetic Shaker was prescribed five times per day. The MD Anderson Dysphagia Inventory (MDADI) served as the sole outcome measure and was administered on average at nine months following completion of treatment

¹ Only some patients were prescribed falsetto phonation. The authors did not indicate why.

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for the pre-treatment group and 14 months, on average, for the post-treatment group. Overall, MDADI scores as well as individual domain scores were compared between the two groups. The pre-treatment group had significantly better overall MDADI scores than the concurrent-treatment group as well as significantly better physical and emotional domain scores. Functional domain scores followed the same trend but did not reach significance ($p = .114$).

Three significant limitations exist for Kulbersh (2006). First, the participants were not randomly assigned and hence, the groups were unbalanced. Second, outcome assessment times differed. The average assessment time for the pretreatment group was nine months, while the average assessment time for the control group was 14 months. Delayed effects of radiation (i.e., fibrosis) may have affected the control group MDADI scores (O'Sullivan & Levin, 2003). Thirdly, Kulbersh did not report compliance data; nor did he report that he controlled for differences in compliance between the two groups. Given the relatively close onset times of PSE for the two groups, and the small sample sizes (particularly for the control group), controlling for compliance differences between the two groups is essential to isolate the effects of PSE initiation timing.

Van der Molen et al. (2011) expanded on efficacy of prophylactic dysphagia intervention by investigating two different types of prophylactic exercise programs using a randomized control trial design. Each program consisted of range of motion stretches and strengthening exercises. The “standard” group ($n = 25$) was prescribed range-of-motion exercises for the jaw and tongue and four strengthening exercises – gargle, effortful swallow, Masako maneuver, and super-supraglottic. The “experimental” group ($n = 30$) was prescribed stretch exercises for the jaw using the Therabite device and a suprahyoid strengthening exercise consisting of “swallowing with the tongue elevated to the palate while maintaining mouth opening at 50% of its maximum” (p. 159). The participants began exercises two weeks prior to the onset of CRT and were instructed to perform the exercises three times

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per day. Three repetitions were prescribed per exercise session for each of the exercises, except for the ROM exercises, which were prescribed for five repetitions. Outcome measures were taken prior to CRT and approximately 10 weeks following completion of CRT. Measures included MBS, maximum inter-incisor mouth opening (MIO), weight, body mass index (BMI), the functional oral intake scale (FOIS), a study-specific questionnaire on quality-of-life, and a visual analog scale for pain assessment (presumably swallowing pain). Specific measures obtained from the MBS included the penetration-aspiration scale (PAS) and the presence or absence of contrast residue in the pharynx. Group comparisons revealed only one difference; the experimental group had less residue on cake at 10 weeks post-CRT than the standard group. An effect size was not reported, preventing any conclusions regarding the extent of the difference. This relative lack of group differences is particularly interesting in that the patients in the standard group were significantly more compliant with their exercises than those in the experimental group²; yet, the only significant outcome difference favored the experimental group.

Several weaknesses of van der Molen et al. (2011) are evident. First, a no-PSE treatment control group was not included. The authors point out that this “could not be avoided since withholding rehabilitation is no longer considered ethical according to the guidelines of the Dutch Head and Neck Cooperative Group” (p. 162). This rationale is certainly legitimate; however, without a no-PSE treatment control group, and given the minimal differences between the groups, and lack of reported effect size on the one difference found, it is difficult to conclude that either exercise program was efficacious, or to what extent either program was of benefit. The authors did include a discussion of how their results compared to other studies in the literature that included no-treatment control

² The mean total days patients practiced the exercises for both groups was 50 out of an approximate 120-day observation period. Mean = 59 days and 41 days for the standard and experimental groups, respectively ($p = .05$).

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groups. Their results were favorable to other studies in regards to PAS scores (Carroll et al., 2008) and weight change (Newman et al., 1998; Oates et al., 2007). Additionally, feeding-tube dependency rates at the end of treatment (76%) and 10-weeks post treatment (37%) were better than similar randomized studies done at their institution, which showed an average of 86% tube-dependency at the end of treatment and 62% tube-dependency at 12 weeks post-treatment (Ackerstaff et al., 2009). A second weakness of the study is that the patients were only assessed at 10 weeks post-CRT, so differences between the groups before or after that period is unknown. Lastly, and potentially most importantly, although the exercises in the standard group were similar to that of Carroll et al. (2008) and Kulbersh (2006), the dosage of the exercise programs was quite different. Carroll et al. and Kulbersh prescribed 10 repetitions five times per day, whereas van der Molen et al. prescribed 3-5 repetitions, three times per day. The differences between van der Molen et al.'s exercise protocols should also be considered in light of the differences in dosage. Van der Molen et al.'s experimental exercise program targeted primarily ROM of the jaw with only one exercise targeting swallowing strength, whereas the standard exercise protocol consisted of four swallowing strength exercises. Further, the experimental strength exercise was intended to target only suprahyoid muscles, whereas the standard strength exercises targeted tongue-base retraction and pharyngeal contraction. Given that tongue-base retraction and pharyngeal contraction are two of the most common pathophysiological impairments in patients with HNC treated with RT/CRT (Frowen & Perry, 2006; Hutcheson et al., 2008; Kotz et al., 2004; Logemann et al., 2008) it is surprising that a protocol that did not target either of these two swallowing functions was better than a protocol that did target these functions. It may be that this expected difference was not found due to the weak dosage of the standard exercises.

Carnaby-Mann and colleagues (2011) published the only PSE study that included assessment of muscle deterioration and composition using T₂-weighted MRI. Their study was a randomized

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control trial that included three groups. Patients in the “usual care” group (n = 20) received sessions with an SLP during RT/CRT for education and monitoring. Patients in the “standard sham” group (n = 18) completed a buccal extension exercise (“valcuff”) twice per day throughout RT/CRT. The third group, termed the “pharyngocise” group (n = 20), completed daily swallowing exercises (4 cycles of 10 reps, 2x/day) throughout RT/CRT that consisted of falsetto phonation, tongue press, effortful swallow, and jaw resistance/strengthening with the Therabite. Outcome measures were administered at baseline, end of CRT, and six months post-treatment. Only 31 participants (approximately 50% of each group) were assessed at six months post-treatment. Measures included MBS, FOIS, Mann Assessment of Swallowing Ability (MASA), smell and taste, saliva production, weight, QOL questionnaires, and T₂-weighted MRI. The pharyngocise group was superior to the usual-care group in regards to muscle deterioration in the genioglossus, mylohyoid, and hyoglossus muscles, oral feeding maintenance, PEG-tube dependence rate, salivary function, taste, and smell. The pharyngocise group also demonstrated less decline in functional swallowing and mouth opening than both the usual-care and sham groups. A significant advantage of this study was the inclusion of a sham PSE group, which controlled for a placebo effect. The primary limitations of the study are: (1) the approximate 50% attrition rate by the six month post-treatment point, for which the authors did not provide a rationale, and (2) the lack of three-month post-treatment data.

Virani et al. (2015) designed the first PSE study to address the problem of PSE compliance. They compared a PSE program consisting of three common PSE swallowing exercises (“exercise group,” n = 26) to a simple and salient program consisting only of repetitive swallowing (“swallow group,” n = 24). The exercise group completed the Masako, pharyngeal squeeze, and shaker exercise. The Masako and pharyngeal squeeze exercises were prescribed at seven sets of 10 repetitions per set daily, while the Shaker exercise was performed at a frequency of three sets per day. Participants in the

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“repetitive swallowing” group were prescribed 34 saliva and/or water swallows seven times per day.

FOIS scores, MDADI scores, and PEG placement rates were compared at baseline, post-treatment, and at three months post-treatment. FOIS and MDADI scores were not significantly different between the groups at any of the data collection points, but PEG tube dependence rates at three months post-treatment were significantly lower in the exercise group than the swallow group, at 16% and 50%, respectively. Compliance rates declined sharply in each group throughout the course of RT/CRT but were not significantly different between the groups. The primary limitations to Virani et al. (2015) include the following: (1) small number of participants, (2) lack of swallowing-pain measure, (3) lack of one month and six month post-treatment data.

To date, one study has shown a lack of support for prophylactic dysphagia intervention in patients with HNC treated with RT/CRT. Ahlberg et al. (2011) performed a prospective, nonrandomized cohort study comparing two groups of patients diagnosed with HNC and treated with RT. The experimental group (n = 84) received PSE while the control group (n = 121) did not receive PSE. The prescribed PSE included 10 repetitions of the Mendelsohn maneuver and five repetitions of tongue range-of-motion stretches (out, up, down, laterally), one to two times a day. Experimental participants were also prescribed strengthening and stretch exercises for the head and neck including flexion/active rotation of the head in both directions and lateral flexion/extension of the head. The ‘Acute Medic Jaw Trainer and Stretcher’ was also used to increase jaw range of motion. It was prescribed for 10 repetitions of 20 seconds each, two times per day. The swallowing exercises (Mendelsohn and tongue range of motion) were initiated before RT and continued for three months following RT. The head and neck strengthening and stretch exercises were also initiated before the start of RT but were continued until six months post-RT. Assessment measures used by Ahlberg et al. (2011) included clinical swallowing function, weight changes, two-year survival, health-related quality

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of life (HRQOL), European Organization for Research and Treatment of Cancer (EORTC) questionnaires, Hospital Anxiety and Depression Scale (HADS), project specific questionnaire focused on self-reported functional losses, rehabilitation, and working ability. Measures were taken at baseline and six months post-RT/CRT (aside from two-year survival). Results revealed no positive effects of PSE. Furthermore, compared to patients who did not receive PSE, patients enrolled in PSE reported significantly more swallowing difficulty than those not enrolled in PSE.

Several differences between Ahlberg et al. (2011) and other PSE studies may explain the difference in findings. At first glance, Ahlberg et al.'s large sample sizes and comprehensive outcome measures indicate a significant strength over the other PSE studies; however, other differences reveal weaknesses of Alberg et al.'s methodology and may explain the lack of apparent benefit of PSE. First is the issue of dosage. Ahlberg et al. recommended two swallowing exercises (Mendelsohn and tongue range of motion), whereas each of the other PSE studies recommended three to five swallowing exercises. Additionally, Ahlberg et al. recommended only five to 10 repetitions of each exercise, one to two times daily. Other PSE studies prescribed either multiple sets of each exercise, or to perform each exercise three to five times a day. Overall, this is a significant difference in dosage and the lack of differences in swallowing outcomes in the Ahlberg et al. study may be due to insufficient intensity of the PSE program.

An additional difference between Alberg et al.'s study and the other PSE studies is the proportion of patients with stage I or stage II cancer, and the proportion of patients who received adjunctive chemotherapy. Approximately 30% of the patients included in Alberg el al.'s study had stage I or stage II cancer, and only 23% of the participants received adjunctive chemotherapy. The other PSE studies included primarily patients with stage III or IV cancer³ and nearly all patients

³ Carbaby-Mann et al. (2011) did not report cancer stage of their participants.

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received adjunctive chemotherapy. Given that severity of RT/CRT toxicity-induced dysphagia is directly related to RT dose and adjunctive chemotherapy worsens the negative effects of RT (Forastiere et al., 2001), a disproportionate amount of patients getting lower doses of RT and no chemotherapy may have impeded a finding of group differences between the control and experimental groups in patients with advanced HNC.

Several themes emerge from a review of previous PSE studies. These themes provide direction for future research and informed the current study. First, significant methodological variations are apparent across previous PSE studies, which impedes valid cross-study comparisons and reproducibility of results. Methodological differences include timing of onset of PSE, exact PSE exercises prescribed, differences in dose and dose frequency, and differences in data collection times. Second, although numerous studies confirm that QOL is reduced in patients with HNC, and QOL is related to swallowing function and swallowing pain, few previous studies were designed with QOL in mind. Some previous studies looked at QOL post RT/CRT but no previous studies attempted to create a PSE program that minimizes swallowing pain to minimize impacts on QOL during RT/CRT. Lastly, every PSE study that discussed compliance reported it to be a problem, and Kotz et al. (2012) reported anecdotally that patients reported that one of the primary reasons for poor compliance was mouth and throat pain.

The current study addressed three of these problems: (1) this study used similar methodology to other PSE studies in regards to exercises and dosage (Carnaby-Mann et al., 2011; Carroll et al., 2008; Kotz et al., 2012; Kulbersh, 2006; Virani et al., 2015), outcome measures (Carnaby-Mann et al., 2011; van der Molen et al., 2011; Virani et al., 2015), and schedule for collecting outcome measures (Carnaby-Mann et al., 2011; Kulbersh, 2006; Virani et al., 2015); (2) this study included a validated swallowing-related QOL instrument (the MDADI) to capture changes in swallowing-related QOL; and

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(3) this study addressed the problem of compliance by contrasting a PSE program consisting solely of indirect (i.e., non-specific) swallowing exercises (exercises that do not require actual swallowing) to a PSE program consisting of a combination of indirect and direct (i.e., specific) swallowing exercises (exercises that require swallowing) in an attempt to create an effective program that minimizes patient discomfort and maximizes patient compliance. The program consisting of both direct and indirect exercises was very similar to previous PSE studies and served as the comparison group.

Table 1

Summary of prior studies on prophylactic swallowing exercises and key findings

Authors	N	Exercises	Dose/Dose Frequency	Outcome measures	Compliance	Key Findings
Carroll et al. (2008)	9 treatment 9 no-treatment control	Mendelsohn Masako Tongue resistance Effortful swallow Shaker	10 reps, 5x/day Shaker: 1 set/day	1. MBS at 3 months post 2. G-tube status at 12 mo	Not reported	Significant improvement in epiglottic inversion and tongue base position in the PSE group. No difference in G-tube removal time between groups.
Kotz et al. (2012)	10 treatment 11 usual care (no-tx)	Effortful swallow Super-supraglottic swallow Tongue-hold maneuver Tongue retraction Mendelsohn maneuver	10 reps, 3x/day	Pre-RT, 3, 6, 9, and 12 mo post-RT: 1. PSS-HN 2. FOIS	~70% ceased exs by week 5 due to pain and fatigue	Better swallowing function in PSE pts at 3 and 6 mo post-RT but not immediately post-RT or at 12 mo.
Kulbersh et al. (2006)	25 treatment (exs onset 2 wks pre-RT) 12 control (exs onset first RT)	Mendelsohn Masako Tongue resistance Falsetto voice (only a few pts) Shaker	10 reps; 5x/day Shaker: Isometric: 3x/day Isokinetic: 30 reps, 5x/day	MDADI at 6 to 12 mo (median=9 mo)	Not reported	Improved MDADI scores in the PSE group
van der Molen et al. (2011)	25 Standard 25 Experimental	Jaw and tongue ROM Gargling Masako Super-supraglottic Therabite stretch Therabite swallow	Stand: ROM: 3 reps, 3x/day Others: 5reps, 3x/day Exp: Stretch: 3 reps, 3x/day Swallow: 10 reps, 3x/day	Pre-RT, 10 wk post-RT: 1. MBS (PAS) 2. Maximum interincisor opening 3. Weight change 4. BMI 5. FOIS 6. Study-specific questionnaire	Avg compliance of 40% overall. Female > men. Stand grp > exp grp	Significantly less cookie residue after treatment in exp group. No significant difference between the groups in PAS

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				7. Visual analog scale for pain		
Carnaby-Mann et al. (2011)	20 usual care	No treatment	4 sets of 10 reps, 2x/day (sham and pharyngocise)	Pre-tx, post-tx, and at 6 mos post-tx:	68% on avg overall; better compliance in sham group	Greater perseveration of genioglossus, mylohyoid, and hyoglossus in pharyngocise group. No sig difference on FOIS or MBS. Less functional decline in swallowing (MASA score) in pharyngocise than usual care and sham groups. Better mouth opening and saliva in pharyngocise group than both sham and usual care groups.
	18 sham	Valchuff		1. T2-weighted MRI		
	20 pharyngocise	Falsetto, tongue press, hard swallow, therabite		2. MBS 3. FOIS 4. MASA 5 Mouth opening 6. Saliva 7. Smell and taste		
Virani et al. (2015)	26 repetitive swallow	Repetitive swallows	7 sets of 34 swallows daily	Pre-tx, post-tx, 3 months post-tx:	Gradual decline in both groups throughout	Sig. less PEGs in exs group at 3 mos post-tx across all patients. Sig. less PEGs in exs group at post-tx and 3 months in patients who received CRT. No difference in FOIS or MDADI scores.
	24 exercise	Masako Pharyngeal squeeze Shaker	7 sets of 10 reps/set daily Shaker: 3x/day	1. FOIS 2. MDADI 3. PEG placement	RT/CRT. Less than 60% by week 6	
Ahlberg et al. (2011)	190 exp group	Oral tongue ROM/stretch	5 reps, 1-2x/day	Pre-tx and 3 months post-tx:	Not reported	No sig difference in weight loss or functional measures. Patients in exp group complained of swallowing difficulty more than those in no-tx group.
	184 no-treatment	Mendelsohn Acute Medic JTS Stretching exs	10 reps/1-2x/day 10x20 sec, 2x/day 3x10, 2x/day	1. Clinical swallow eval 2. Weight 3. Tongue, head, neck ROM 4. Interincisor opening 5. 3 QOL measures 6. HADS 7. Study-specific questionnaire		

Note: exp = experimental; CRT = chemoradiotherapy; FOIS = functional oral intake scale; HADS = Hospital Anxiety and Depression Scale; MASA = Mann Assessment of Swallowing Ability; MBS = modified barium swallow; MDADI = MD Anderson Dysphagia Inventory; MRI = magnetic resonance imaging; mo = month(s); PAS = penetration-aspiration scale; PEG = percutaneous endoscopic gastrostomy; PSS-HN = Performance Status Scale for Head and Neck Cancer; QOL = quality of life; RT = radiotherapy; reps = repetitions; pts = patients; sig = significant; tx = treatment.

Chapter 3: Methodology

The Joint Investigational Review Board (JIRB) at Saint Patrick's Hospital and Community Medical Center as well as The University of Montana IRB approved this non-randomized prospective study on September 16, 2012. The study was in collaboration with the radiation oncologists at the Montana Cancer Center within Providence St. Patrick Hospital in Missoula, MT (Dr. Kathryn Markette, Dr. Margaret Menendez, and Dr. Jeffrey Stephenson), and Community Cancer Center in Missoula, MT (Dr. Michelle Proper), as well as the otolaryngologists at Rocky Mountain Ear, Nose, and Throat Center (Dr. Jeffrey Haller, Dr. Daniel Braby, Dr. Phillip Gardner). Data collection commenced from September 2012 to July 2015.

Recruitment

The primary role of the aforementioned physicians was participant recruitment. The physicians informed patients that met the inclusion criteria of the study. Patients who were interested in learning more about the study filled out a simple contact-consent form, which was then faxed to the principal investigator (see Appendix A). Patients were then contacted to set up an appointment in order to review the study protocol. All participation was voluntary.

The following inclusionary criteria were used to enroll patients:

- 1) patients were diagnosed with stage III or IV squamous cell carcinoma of the tongue, palate, pharynx, or larynx;
- 2) patients were treated with radiation with or without adjunctive chemotherapy (RT/CRT);
- 3) patients were able to begin PSE exercises prior to the onset of RT/CRT;
- 4) patients were at least 18 years of age;

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- 5) patients were cognitively, mentally, and legally capable of making independent decisions regarding his/her personal medical care;

The following exclusionary criteria were used:

- 1) patients 18 years of age were excluded;
- 2) patients who had undergone previous radiation treatment to the mouth, pharynx, or larynx were excluded;
- 3) patients with a treatment including surgical dissection to the primary tumor were excluded if the surgical dissection resulted in dysphagia;
- 4) patients suffering from dysphagia unrelated to the current cancer diagnosis were excluded;
- 5) patients with any disease process other than their current HNC diagnosis that may have caused dysphagia were excluded (e.g., progressive neurological disease).

Measures

Instrumental swallowing assessment. Each participant underwent a baseline instrumental swallow evaluation (i.e., MBS or FEES) to determine baseline swallowing function. A staff SLP and staff radiologist at St. Patrick's Hospital or Community Medical Center Radiology departments performed the MBS exams. The protocol for each MBS was at the discretion of the SLP administering the exam. If for some reason the patient could not, or did not wish to, participate in the MBS, the participant underwent a FEES study. All FEES exams were completed at The University of Montana Voice and Swallow Clinic by the principal investigator.

Study-specific nutrition and pain questionnaire. A one-page study-specific questionnaire was designed to obtain information on weight, oral intake measures (e.g., percent feeding tube use) and swallowing-related pain. This questionnaire can be seen in Appendix B.

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Functional Oral Intake Scale (FOIS): The Functional Oral Intake Scale (FOIS) is a 7-point scale of oral diet tolerance. It ranges from complete feeding tube dependence (level 1) to a full oral diet without restriction or compensation (level 7). The FOIS was validated in the stroke population, which revealed excellent levels of inter-rater reliability (.86 to .91) and high consensual validity (.90). Criterion validity was also high at onset ($r = .31$ to $.53$) and at one month post-stroke ($r = .46$ to $.76$), relative to two measures of stroke severity and one measure of swallowing function. Additionally, the FOIS was associated with dysphagia severity ($r = .54$) and aspiration severity ($r = .30$) as measured by the modified barium swallow study (Crary, Mann, & Groher, 2005). The FOIS has been used in three previous prophylactic swallowing studies (Carnaby-Mann et al., 2011; van der Molen et al., 2011; Virani et al., 2015). For the purposes of this study the FOIS was added to the nutrition and pain questionnaire (see Appendix B).

MD Anderson Dysphagia Inventory (MDADI). The MDADI is a self-administered, Likert-type questionnaire designed and validated specifically for evaluating the impact of dysphagia on psychosocial QOL in patients treated for HNC. It consists of 20 items and has global, emotional, functional, and physical subscales. An overall reliability coefficient of .96, test-retest reliability correlations for each subscale of .69 (global), .88 (emotional), .88 (functional), and .86 (physical), and criterion validity correlations of .47 to .61 indicate that it is an acceptable tool (Chen et al., 2001). The MDADI was added partway through the study after further inspection of the literature indicated the importance of a measure of QOL. The MDADI was chosen over other validated QOL instruments because of its specificity to swallowing-related QOL, its ease of administration, and because it was used in two prior PSE studies (Kulbersh, 2006; Virani et al., 2015), which allowed for additional cross-study comparisons. Because of its late addition to the study, the MDADI was not collected during the treatment-phase for the first six patients. The MDADI can be found in Appendix C.

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Eating Assessment Tool-20 (EAT-20). The EAT-20 is a symptom-specific, Likert-type, 20-item survey instrument used to assess patient-reported dysphagia symptoms. Original reliability testing of the EAT-20 revealed test-retest reliability for each single item ranging from .689 to .958 with the exception of one item, which scored .383 (Belafsky et al., 2008). Belafsky et al. (2008) then eliminated the 10 items with the lowest test-retest reliability resulting in a 10-item survey (EAT-10). The current study used the EAT-20 rather than the EAT-10 because initial data for the current protocol was obtained with the EAT-20 rather than the EAT-10. One advantage of the EAT-20 is that many of the items contained in it, but eliminated from the EAT-10, speak to the impact of dysphagia on QOL (e.g., “I’m afraid to eat because of my swallowing problem.” “I’m afraid of choking in my sleep.” “My swallowing problem interferes with my work or other activities.”). These specific items showed test-retest reliability of .689, .780, .866, respectively, on the original testing of the EAT-20 (Belafsky et al., 2008). The EAT-20 can be seen in Appendix D.

Given that many of the items on the EAT-20 spoke to swallowing-related QOL, the researchers chose to divide the EAT-20 into 1) physical, 2) emotional, and 3) functional subscales modeled after the MDADI. A qualitative correlate was created between the questions used in the EAT-20 and the questions listed in the physical, emotional, and functional subscales of the MDADI. Chronbach’s alpha coefficient was then applied to measure internal consistency within the EAT-20 subscales at the third data collection point (i.e., between the patient’s 23-25 RT treatment) and one month post-RT/CRT. Chronbach’s alpha scores were also calculated on the MDADI at one month post-RT/CRT as a comparison. Chronbach’s alpha scores for the EAT-20 ranged from .746 and .958, which are considered acceptable levels of internal consistency (Peterson, 1994). MDADI Chronbach’s alpha scores ranged from .659 to .827. The EAT-20 items in the physical, emotional, and functional subscales are provided in Table 2. Table 3 details the results of the reliability analysis.

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Table 2

EAT-20 items separated into physical, emotional, and functional subscales

Item number	Item description
<u>Physical</u>	
1	My swallowing problem has caused me to lose weight.
4	Swallowing liquids takes extra effort.
5	Swallowing solids takes extra effort.
6	Swallowing pills takes extra effort.
8	Swallowing is painful.
10	When I swallow food sticks in my throat.
11	When I swallow food sticks in my chest.
12	I cough when I eat.
15	I get tired when I eat.
18	I become short of breath when I eat.
<u>Emotional</u>	
9	The pleasure of eating is affected by my swallowing.
13	I am afraid to eat because of my swallowing problem.
14	My swallow problem is a burden to my family.
16	I avoid eating in front of people.
17	I'm afraid of choking in my sleep.
19	People perceive me as sick because of my swallowing problem.
20	Swallowing is stressful.
<u>Functional</u>	
2	My swallowing problem interferes with my ability to go out for meals.
3	My swallowing problem interferes with my work or other activities.
7	I have altered my diet because of my swallowing problem.

Table 3

Chronbach's alpha coefficient measuring internal consistency within the EAT-20 sub-sets (physical, emotional, functional) at baseline and one month post-RT/CRT

	EAT-20 Chronbach's α coefficients	MDADI Chronbach's α coefficients
<u>During RT (data 3)</u>		
Physical	.924	NA
Emotional	.845	NA
Functional	.814	NA
<u>1 Month Post-RT/CRT</u>		

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Physical	.958	.659
Emotional	.746	.827
Functional	.779	.749

Procedures

Following review and signing of the informed consent form and the Health Insurance Portability and Accountability Act (HIPAA) release form (found in Appendices E and F), enrolled patients were placed into one of two prophylactic swallowing exercise (PSE) groups: 1) PSE that consisted of a combination of direct and indirect swallowing exercises (C-PSE), or 2) PSE that consisted solely of indirect swallowing exercises (ID-PSE). Alternate assignment was used, except for the first participant, who was randomly assigned to the C-PSE group.

The exercises for each group were chosen to target pathophysiological impairments common in patients with HNC treated with RT or CRT. As discussed in Chapter 2, they include but are not limited to: reduced tongue-base retraction (Chang et al., 2003; Hutcheson et al., 2008; Kotz et al., 2004; Logemann et al., 2008), reduced tongue strength and/or control (Lazarus et al., 2000; Logemann et al., 2008), reduced range of motion of the jaw (M. L. Kent et al., 2007; Tang et al., 2011), weak pharyngeal contraction (Chang et al., 2003; Logemann et al., 2008), reduced laryngeal elevation and/or excursion (Chang et al., 2003; Hutcheson et al., 2008; Kotz et al., 2004; Logemann et al., 2008; Pauloski, 2008), and reduced or shortened opening of the UES (Hutcheson et al., 2008; Kotz et al., 2004; Logemann et al., 2008; Smith et al., 2000). Reduced epiglottic inversion is also listed as a common impairment (Chang et al., 2003; Hutcheson et al., 2008); however, it is relevant to point out that epiglottic inversion is a result of hyolaryngeal elevation and excursion. As such, it can only be targeted by targeting hyolaryngeal elevation/excursion. In addition to choosing exercises that target common pathophysiologic impairments, each of the exercises chosen were also used in previous prophylactic dysphagia treatment studies, to allow cross comparison with prior published studies. Table 4

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summarizes the common pathophysiologic impairments in patients undergoing RT/CRT for HNC, the swallowing exercises that targeted each impairment in each treatment group, and the swallowing exercises used in prior PSE studies.

Table 4

Common pathophysiologic impairments due to RT/CRT toxicity, the exercises per group that target them, and the prior PSE studies that have included each of the exercises

Pathophysiologic Target	C-PSE Exercise	Prior PSE studies including the exercise	ID-PSE Exercise	Prior PSE studies including the exercise
Tongue-base retraction	Effortful swallow	Carnaby-Mann et al., Carroll et al., Kotz et al.,	Tongue pull-back	Kotz et al.
Tongue strength/control	Effortful swallow	Carnaby-Mann et al., Carroll et al., Kotz et al.	Tongue ROM	Ahlberg et al., van der Molen et al.,
Jaw ROM	Not targeted	NA	Jaw stretch	Ahlberg et al., Carnaby-Mann et al., van der Molen et al.
Pharyngeal contraction	Effortful swallow	Carnaby-Mann et al., Carroll et al., Kotz et al.,	Pharyngeal squeeze	Kulbersh et al., Carnaby-Mann et al., Virani et al.,
	Masako	Carroll et al., Kotz et al., van der Molen et al., Virani et al.,		
Hyolaryngeal elevation/excursion	Mendelsohn	Ahlberg et al., Carroll et al., Kotz et al., Kulbersh et al.,	Pharyngeal squeeze	Kulbersh et al., Carnaby-Mann et al., Virani et al.,
	Shaker	Carroll et al., Kulbersh et al., Virani et al.	Shaker	Carroll et al., Kulbersh et al., Virani et al.
UES opening	Mendelsohn	Ahlberg et al., Carroll et al., Kotz et al., Kulbersh et al.,	Shaker	Carroll et al., Kulbersh et al., Virani et al.
	Shaker	Carroll et al., Kulbersh et al., Virani et al.		

Note: NA not applicable, ROM range of motion, UES upper esophageal sphincter

Dosage for each exercise was determined based on previous PSE studies, efficacy literature (when available), and clinical experience. Regarding dose frequency (i.e., number of treatment sessions per day), Carroll et al. (2008) and Kulbersh et al. (2006) prescribed PSEs five times per day while Kotz et al. (2012), van der Molen et al. (2011) and Virani et al. (2015) prescribed PSEs three times per day.

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Given that exercise volume and inconvenience have been shown to impact compliance (Pollock et al., 1998; Sluijs, Kok, & Zee, 1993), we felt that a frequency of three times per day was more appropriate than five times per day. Repetitions per exercise session were adjusted when necessary to be comparable to prior PSE studies that used a dose frequency of five times per day, so that the total daily intensities were comparable.

Combination Prophylactic Swallowing Exercises (C-PSE). Patients in the C-PSE group were prescribed the following exercises: Mendelsohn, effortful swallow, Masako, and Shaker. The Mendelsohn was prescribed for 15 repetitions, three times per day (Carroll et al., 2008; Kulbersh, 2006). The effortful swallow was prescribed for 20 repetitions, three times per day (Carroll et al., 2008). The Masako was prescribed for 10 repetitions, three times per day (Kotz et al., 2012; van der Molen et al., 2011). The Shaker exercise consisted of one, one-minute hold, a rest period, then 20 repetitions without any hold time (Kulbersh, 2006; Shaker et al., 2002; Virani et al., 2015). The Shaker was also prescribed three times per day. The instructional handout provided to each patient can be found in Appendix G.

Indirect Prophylactic Swallowing Exercises (ID-PSE). Patients in the ID-PSE group were prescribed the following exercises: pharyngeal squeeze (i.e., falsetto “ee”), tongue-base retraction (i.e., finger-assisted tongue pull-back), lingual ROM, jaw ROM, and Shaker exercise. The pharyngeal squeeze exercise was prescribed for six repetitions, three times per day⁴. The tongue-base retraction and ROM exercises were each prescribed for 10 repetitions, three times per day (Kotz et al., 2012;

⁴ Given that typical maximum phonation time (MPT) is approximately 20 seconds for adults (R. Kent, Kent, & Rosenbek, 1987), patients who were not able to sustain phonation for at least 15 seconds, were prescribed 7- 10 repetitions of the pharyngeal squeeze exercise.

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Logemann et al., 1997). The Shaker exercise was prescribed as described above⁵. The instructional handout that was provided to each patient can be found in Appendix H. The study commenced in three phases.

Training Phase. The training phase began with enrollment and ended the first day of RT/CRT. During the training phase, baseline data was collected including MBS or FEES, study-specific pain and nutrition questionnaire, FOIS, EAT-20, and the MDADI. Participants were also instructed in their exercise program and provided a written instruction handout as well as a paper tracking form for tracking compliance. Participants were seen for as many visits as necessary to verify that they thoroughly understood the program and could accurately execute the exercises independently. All participants were able to achieve independence within one to two sessions. Every effort was made to begin the swallowing exercises up to, but no more than, two weeks prior to RT/CRT onset; however, patients were accepted as long as they were able to begin PSE within one day of RT/CRT onset. Patient handouts and tracking forms for each exercise can be found in Appendices G through J.

Treatment phase. The treatment phase began on the first day of the patient's RT/CRT and continued until the final day of RT/CRT, generally 7-9 weeks. During the treatment phase, the investigators convened with each patient once during radiation doses 12 to 14, once during radiation dose 23 to 25, and on the last day of RT/CRT. The nutrition and pain questionnaire, EAT-20, and MDADI were completed during each of these sessions. The data was collected either immediately before or immediately after RT for that day, at the preference of the patient.

Post-treatment phase. The post-treatment phase consisted of the first six months following completion of RT/CRT. The investigator encouraged each patient to continue PSEs as prescribed

⁵ The Shaker exercise was assigned to both groups at the clinical judgment of the principal investigator, given its high validity for improving hyolaryngeal elevation/excursion and upper esophageal function, both common impairments in HNC patients. (Easterling et al., 2005; Mepani et al., 2008; Shaker et al., 2002)

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during the post-treatment phase until they were able to resume full P.O. intake with minimal dysphagia symptoms. During the post-treatment phase, the investigator phoned each patient every one to two weeks to ensure recovery was occurring as expected. The investigator intended to request an appointment with the patient if he/she reported significant signs or symptoms of aspiration, or any other concerning complaints; however this this was not necessary for any of the patients who continued in the study. The nutrition and pain questionnaire, FOIS, EAT-20, and MDADI were collected at one month and three months post RT/CRT treatment. Most data was gathered over the phone unless the patient requested a paper-based survey be sent in the mail.

Participants

Twenty-four patients attended an initial meeting to review the protocol. Twenty-two patients met the inclusion criteria and enrolled in the study. One patient voluntarily dropped from the study within the first two weeks of enrollment. He stated that he did not feel he would be compliant with the study procedures or exercises. Three patients were dropped due to unwillingness/inability to provide data in line with the study protocol timeline and/or unwillingness or inability to complete an instrumental swallow study. One patient did not respond to a request for one month post-treatment data, four patients did not respond to a request for three month post-treatment data. Additionally, at the time of the current analysis, one patient was not yet at three months post-treatment point. This left a total of 18 patients at one month post-treatment and 14 patients at three months post-treatment. Figure 1 provides a breakdown of participant counts at each data collection time point.

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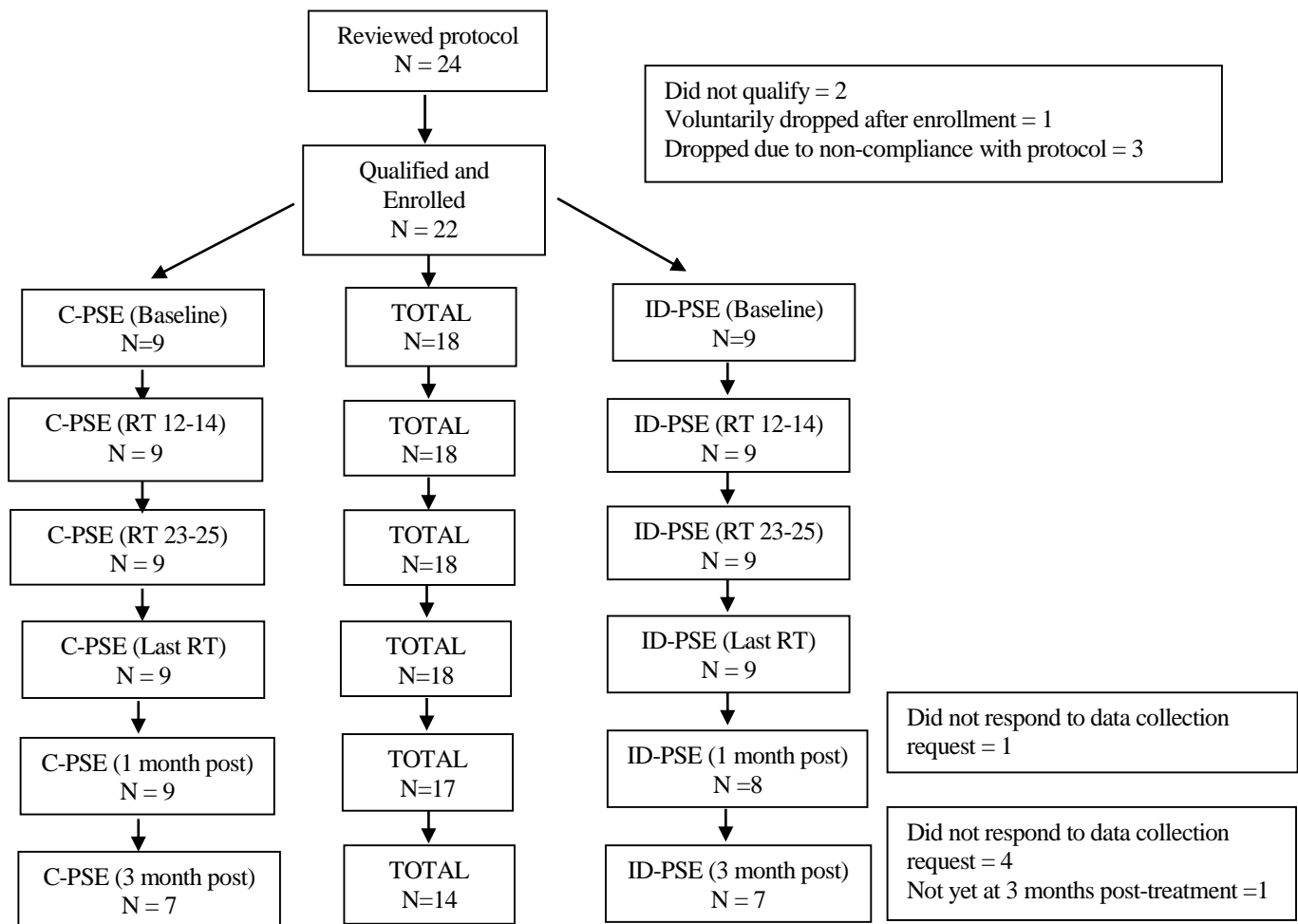


Figure 1. Breakdown of patient enrollment and attrition at each data time point.

Group Demographics and Cancer Characteristics

Table 5 catalogs demographic data and cancer characteristics including *tumor site*, *tumor size* (i.e., T1, T2, T3, or T4, T4 being the worst), *nodal disease* category (i.e., N1, N2, or N3, N3 being the worst) and *cancer stage* (i.e., III or IV, IV being the worst). Between-group differences were analyzed with the Mann-Whitney U test for ordinal and continuous variables and the Fisher's exact test for nominal variables. There were no significant between-group differences on all demographic variables and cancer characteristics. A total of 15 males and three females completed the initial phase of the study. The mean age for the C-PSE group was 60.78 years, with a range of 50-74 years. The mean age

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for the ID-PSE group was 60.22 years, with a range of 50-62 years. The mean age in years for the total population was 60.50, with a range of 45-74. The majority of patients in both groups had a tumor size of T1 or T2 (i.e., 6 out of 9 for both groups). The C-PSE group had two patients with T3 tumors and one patient with a T4 tumor; while the three remaining patients in the ID-PSE group had T3 tumors. All patients in the ID-PSE group had nodal scores of N2. Two patients in the C-PSE group had nodal scores of N1 and one patient had a nodal score of N3. All remaining patients in the C-PSE group had a nodal score of N2. Every patient had stage III or stage IV cancer. Eight patients in the ID-PSE group and seven patients in the C-PSE group had stage IV cancer. Every patient's primary tumor was located in the base of the tongue, tonsil, epiglottis, larynx, or oropharynx with a relatively equal distribution in each group. Every patient was treated with CRT except for one patient in the ID-PSE group who was treated with RT alone.

Table 5

Demographics and baseline data of participants including age, gender, tumor size, nodal disease, cancer stage, tumor site, PEG use, FOIS, EAT-20 scores at baseline. Standard deviations in parentheses where applicable

Variables	C-PSE Group	ID-PSE Group	Total	Test-Statistic	p-value (2-tailed)
No. of Patients	9	9	18	NA	NA
Age					
Mean Age	60.78 (8.48)	60.22 (8.43)	60.50 (8.21)	Mann-Whitney U	.796
Range	50-74	45-74	45-74		
Sex					
Male	8 (89%)	7 (78%)	15 (84%)	Fisher's Exact Test	.712
Female	1 (11%)	2 (22%)	3 (17%)		
Tumor Size					
T1	3 (33%)	3 (33%)	6 (33%)	Mann-Whitney U	.406
T2	3 (33%)	3 (33%)	6 (33%)		
T3	2 (22%)	3 (33%)	5 (28%)		
T4	1 (11%)	0 (0%)	1 (6%)		

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Nodal disease					
N1	2	0	2	Mann-Whitney U	.540
N2	6	9	15		
N3	1	0	1		
Cancer Stage					
Stage III	2 (22%)	1 (11%)	3 (17%)	Fisher's Exact Test	.712
Stage IV	7 (78%)	8 (89%)	15 (83%)		
Tumor site					
Tonsil	3 (33%)	2 (22%)	5 (28%)	Mann-Whitney U	.406
Base of tongue	4 (44%)	3 (33%)	7 (39%)		
Epiglottis	1 (11%)	2 (22%)	3 (17%)		
Oropharynx	0 (0%)	1 (11%)	1 (6%)		
Larynx	1 (11%)	1 (11%)	2 (11%)		
Treatment					
RT alone	0 (0%)	1 (11%)	1 (6%)	Fisher's Exact Test	.500
CRT	9 (100%)	8 (89%)	17 (94%)		
Mean Exs days pre-RT/CRT	11.56 (6.56)	16.78 (12.99)	14.17 (10.34)	Mann-Whitney U	.399

Note: CRT = chemoradiotherapy; Exs = exercises; FOIS = functional oral intake scale; PEG = percutaneous endoscopic gastrostomy; RT = radiotherapy

Baseline Outcomes

Table 6 summarizes baseline outcome data including percentage PEG use, swallowing pain, FOIS, and EAT-20. The MDADI is not included due to baseline data missing for six patients. Essentially all patients had functional swallowing and minimal complaint of swallowing difficulty at baseline except for patient 13 in the ID-PSE group who had severe dysphagia at baseline due to the size of her tumor. This patient was subsequently 100% PEG-tube dependent at baseline and scored 2-4 standard deviations outside the mean on all baseline measures (Table 7). This resulted in higher baseline scores on all measures in the ID-PSE group relative to the C-PSE group. This difference was not statistically significant. Every other patient reported functional swallowing at baseline. Swallowing pain was scored on a scale from 0-5, with 0 being no pain and 5 being the worst pain. Mean swallowing pain at baseline was .78 and .89 for the C-PSE and ID-PSE groups, respectively. The FOIS

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is scored on a 1-7 scale with 1 being fully dependent on a feeding tube and able to take nothing by mouth and 7 being able to eat an oral diet without any restrictions. Mean baseline FOIS scores were 6.89 and 6.11 for the C-PSE and ID-PSE groups, respectively. EAT-20 scores followed a similar pattern with the mean EAT-20 Total score being 20.11 for the ID-PSE group and 3.78 for the C-PSE group. Table 6 catalogues mean baseline scores on each outcome measure.

Table 6

Baseline outcome data including percentage PEG use, swallowing pain, FOIS, and EAT-20.

Variables	C-PSE Group (n = 9)	ID-PSE Group (n = 9)	Total	Test	p-value (2-tailed)
Mean PEG use (0-5)	0	.56 (1.67)	.278 (1.18)	Mann-Whitney U	.317
Mean swallowing pain (0-5)	.78 (.83)	.89 (1.36)	.83 (1.10)	Mann-Whitney U	.811
Mean FOIS	6.89 (.33)	6.11 (1.97)	6.5 (1.42)	Mann-Whitney U	.248
Mean EAT-20 TOTAL	3.78 (6.61)	20.11 (34.88)	11.94 (25.76)	Mann-Whitney U	.343
Mean EAT-20 Physical	2.78 (4.32)	10.44 (18.53)	6.61 (13.63)	Mann-Whitney U	.523
Mean EAT-20 Emotional	.667 (1.66)	6.11 (11.66)	3.39 (8.55)	Mann-Whitney U	.269
Mean EAT-20 Functional	.33 (.71)	3.56 (5.62)	1.94 (4.22)	Mann-Whitney U	.226

Note: EAT = Eating Assessment Tool; FOIS = Functional Oral Intake Scale; PEG = percutaneous endoscopic gastrostomy tube

Table 7

Total group means contrasted with patient 13's individual scores on baseline measures and the standard deviations away from the total group mean for patient 13

	Total group mean	Patient 13 score	Standard deviations from the mean
Percent PEG use (0-5)	.278 (1.18)	5	4.00
Swallowing pain (0-5)	.83 (1.10)	4	2.88
FOIS (7-1)	6.5 (1.42)	1	3.87
EAT-20 Physical	6.61 (13.63)	56	3.62
EAT-20 Emotional	3.39 (8.55)	33	3.56
EAT-20 Functional	1.94 (4.22)	14	2.86
EAT-20 Total	11.94 (25.76)	103	3.53

Note: EAT-20 = Eating Assessment Tool-20; FOIS = Functional Oral Intake Scale; PEG = percutaneous endoscopic gastrostomy

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In addition to swallowing pain, FOIS, and EAT-20 scores, baseline instrumental swallow study (i.e., modified barium swallow (MBS) or fiberoptic endoscopic evaluation of swallowing (FEES)) results were reviewed. The results of the instrumental studies were consistent with patient reports in that every patient in the entire cohort had functional swallowing ability aside from patient 13 of the ID-PSE group. Patient 13's MBS study confirmed severe aspiration on every consistency and an unsafe swallow. No other patients had aspiration. Three patients in the ID-PSE group and one patient in the C-PSE group had mild penetration without aspiration on thin liquids. Four patient in the ID-PSE group and three patients in the C-PSE group had very mild pharyngeal post-swallow residue that cleared easily with an extra swallow. No other remarkable findings were reported.

Statistical Analysis

All statistical analyses were performed using IBM SPSS v 22 (SPSS, Inc., Chicago, IL) software. Histograms and Q-Q plots of the data revealed evidence of non-normal distributions in a majority of the variables at each time point. Further, the sample sizes were arguably too small to allow accurate assessment of distributional assumptions (Field, 2013a). Inability to determine distributional assumptions necessitated the use of non-parametric tests. The Mann-Whitney U test was chosen as the most appropriate non-parametric test for ordinal and continuous variables. The data met the following assumptions required for the Mann-Whitney U test: 1) the dependent variable was measured at the continuous or ordinal level, 2) the independent variable was dichotomous, and 3) the observations were independent (Mann whitney U test in SPSS.). Further, Pero-Cebollero and Guardia-Olmos (2013) found the Mann-Whitney U test to have the lowest error rate relative to other non-parametric tests that compare two independent groups, particularly with small sample sizes. The correlation coefficient was used as an effect size when using the Mann-Whitney U test (Field, 2013c). The Fisher's exact test was

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used to test between-group differences on nominal variables due to violation of the chi-square distribution assumption (Field, 2013b).

Chapter 4: Results

The purpose of this study was to determine if a prophylactic swallowing exercise (PSE) program consisting solely of indirect swallowing exercises (ID-PSE) results in the following outcomes: 1) better compliance, 2) better oral intake, 3) better swallowing-related QOL, and 4) less swallowing pain than a PSE program consisting of a combination of indirect swallowing exercises and direct swallowing exercises (C-PSE). The precipitance for the study was poor compliance from patients in prior PSE studies that we hypothesized was due to swallowing pain that was exacerbated by direct swallowing exercises.

Compliance

Compliance was tracked with a paper-tracking sheet filled out by each patient at home and returned to the investigator at data collection time points. A compliance percentage was calculated per patient for the pre-RT/CRT phase and each week for weeks 1 to 8 during RT/CRT. Additionally, total compliance for weeks 1 to 4, and weeks 4 to 7 during RT/CRT, as well as an overall compliance was calculated for each group. Compliance for each group declined gradually throughout RT/CRT. Overall compliance was 42% and 47% for the C-PSE and ID-PSE groups, respectively. The C-PSE group began with a mean compliance of 58% in the pre-RT/CRT phase and declined to 39% at week seven. Compliance for the ID-PSE group began at 62% in the pre-RT/CRT phase and declined to 48% at week seven. Mean compliance for the first half of RT/CRT (i.e., weeks 1-4) was 43% and 51% for the C-PSE and ID-PSE groups, respectively. Mean compliance for the second half of RT/CRT (i.e., weeks 4-7) was 38% and 41% for the C-PSE and ID-PSE groups, respectively. Figure 2 depicts compliance rates per group from the pre-RT/CRT phase and weekly through week seven of RT/CRT. The Mann-Whitney U test revealed no statistically significant between-group differences for overall total compliance ($U = 18, z = -.044, p = .50, r = -.01$), compliance during the first half of RT/CRT ($U =$

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18, $z = .353$ $p = .37$, $r = .08$), and compliance during the second half of RT/CRT ($U = 17$, $z = .097$, $p = .50$, $r = .02$). Tables 8-9 and Figures 2-3 depict these results.

Table 8

Mean compliance rates, standard deviations, and ranges pre-RT/CRT and weekly during RT/CRT

	<u>C-PSE</u>			<u>ID-PSE</u>			<u>Groups Combined</u>	
	Compliance (%)	SD	Range	Compliance (%)	SD	Range	Compliance (%)	SD
Pre-RT/CRT	.58	.42	.10-1.0	.62	.36	.15-1.0	.60	.38
Week 1	.50	.37	0-1.0	.58	.38	0-1.0	.54	.36
Week 2	.42	.41	0-1.0	.56	.37	0-.92	.49	.38
Week 3	.43	.43	0-1.0	.49	.39	0-.97	.46	.40
Week 4	.36	.45	0-1.0	.43	.39	0-1.0	.40	.41
Week 5	.39	.47	0-1.0	.38	.44	0-1.0	.38	.44
Week 6	.39	.48	0-1.0	.29	.38	0-1.0	.34	.42
Week 7	.53	.47	0-1.0	.23	.42	0-1.0	.38	.43

Note: SD = standard deviation

Table 9

Mean compliance rates for the first half and second half of the RT/CRT phase as well as total compliance per group. P-value based on the Mann-Whitney U test

	C-PSE	ID-PSE	<i>p</i> -value (1-tailed)
Weeks 1-4	.43	.51	.365
Weeks 4-7	.38	.41	.50
Total	.42	.47	.50

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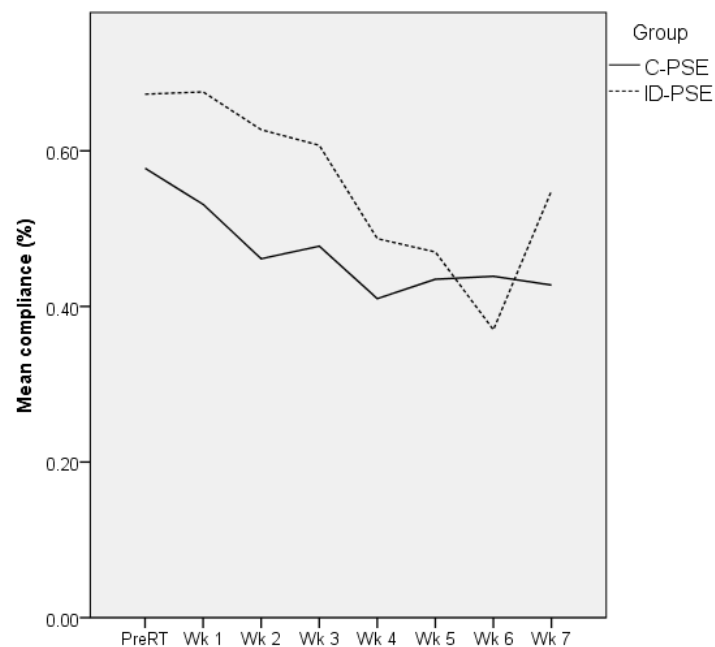


Figure 2. Mean compliance per group from pre-RT/CRT through week seven of RT/CRT

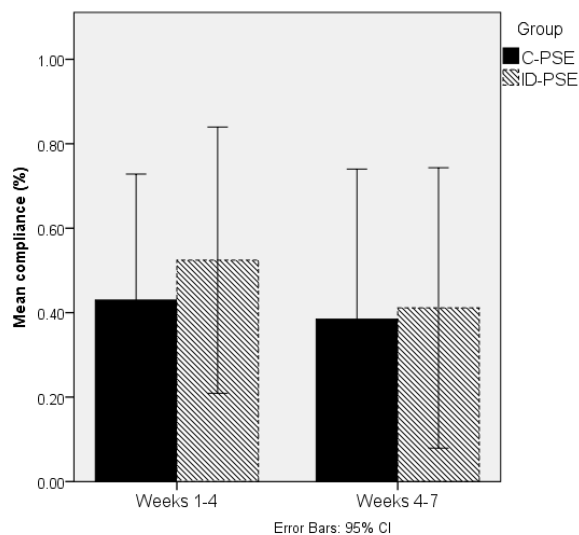


Figure 3. Mean compliance per group for the first and second half of RT/CRT

Oral Intake

Oral intake was measured with percentage PEG tube use and the Functional Oral Intake Scale (FOIS). The patient estimated his/her average PEG tube use relative to his/her total intake

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(i.e., orally and PEG) at the time of each data collection time point using a 0-5 scale (i.e., 0=0-10%; 1 = 10-25%; 2 = 25-50%; 3 = 50-75%; 4 = 75-90%; 5 = 90-100%). The investigator determined the FOIS score based upon what the patient reported he/she was consuming orally. An FOIS score of 7 indicated full oral intake with a non-restrictive diet and a score of 1 indicated complete dependence on the PEG tube. As expected PEG tube use and FOIS scores had an inverse relationship with PEG tube use scores gradually increasing throughout the RT/CRT phase and then gradually decreasing in the post-RT/CRT phase, and FOIS scores gradually decreasing through the RT/CRT phase and then gradually increasing in the post-RT/CRT phase. Mean PEG tube use score for the C-PSE group was 0 at baseline, 3.33 at the final RT session, and .429 at three months post RT/CRT. While mean FOIS score for the C-PSE group was 6.879 at baseline, 3.56 at the final RT session, and 6.14 at three months post RT/CRT. Mean PEG tube use scores for the ID-PSE group were .56 at baseline, 4.11 at the final RT session, and .71 at three months post RT/CRT. Mean FOIS scores for the ID-PSE group was 6.11 at baseline, 2.56 at the final RT session, and 5.86 at three months post RT/CRT. Visual inspection of the data indicated no evidence of a significant difference in FOIS scores between the two groups, but some potential of a significant difference between the two groups for PEG use at RT 23-25 and the end of RT (Figure 4). However, the Mann-Whitney U test revealed no statistically significant between-group differences on PEG use or FOIS scores at any time point. Tables 10 and 11 and Figures 4 and 5 summarize mean PEG use and FOIS scores at each time point.

Table 10

Mean PEG use, standard deviations, and ranges at baseline, RT 12-14, RT 23-25, Final RT, one month post-RT/CRT, and three months post-RT/CRT. Statistical significance by Mann-Whitney U test

	<u>C-PSE</u>			<u>ID-PSE</u>					p-value (1-tailed)
	PEG use	SD	Range	PEG use	SD	Range	U	Effect size	
Baseline	0	0	0	.56	1.67	0-5	36.0	.24	.365
RT 12-14	1.78	2.17	0-5	2.0	2.45	0-5	37.5	-.06	.398
RT 23-25	2.67	2.55	0-5	3.78	2.17	0-5	35.5	-.012	.333
Final RT	3.33	2.5	0-5	4.11	1.83	0-5	34.5	-.15	.303
1 month post	2.0	2.45	0-5	1.88	2.17	0-5	34.5	-.03	.444
3 month post	.429	1.13	0-3	.71	1.89	0-5	31.5	-.02	.479

Note. SD = standard deviation

Table 11

Mean FOIS scores, standard deviations, and ranges at baseline, RT 12-14, RT 23-25, Final RT, one month post-RT/CRT, and three months post-RT/CRT. Statistical significance by Mann-Whitney U test

	<u>C-PSE</u>			<u>ID-PSE</u>					p-value (1-tailed)
	FOIS	SD	Range	FOIS	SD	Range	U	Effect size	
Baseline	6.89	.33	6-7	6.11	1.97	1-7	31.0	-.27	.124
RT 12-14	4.33	1.87	2-7	4.56	2.01	2-7	36.5	-.09	.358
RT 23-25	3.56	2.01	1-6	3.00	1.73	2-6	34.5	-.14	.284
Final RT	2.78	1.99	1-6	2.56	1.01	2-5	35.0	-.12	.301
1 month post	3.89	1.97	1-6	4.75	1.91	3-7	25.0	-.26	.139
3 month post	6.14	1.46	3-7	5.86	1.77	2-7	21.0	-.02	.312

Note. FOIS = Functional Oral Intake Scale; SD = standard deviation

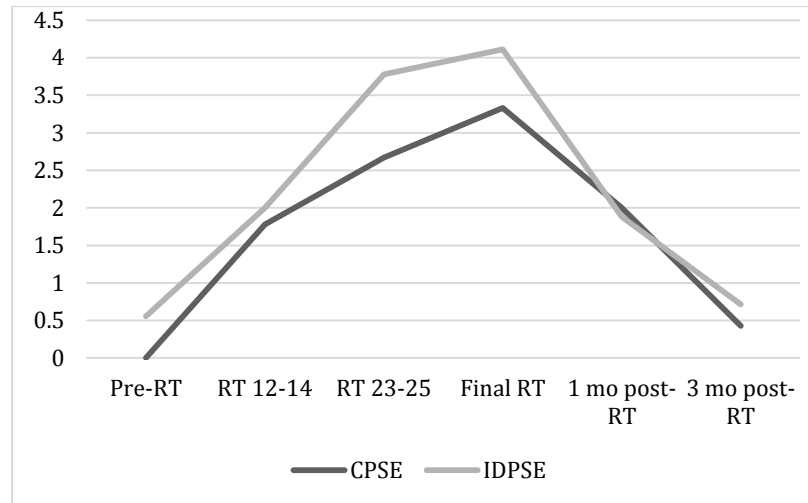


Figure 4. Mean PEG tube use from baseline to three months post-RT/CRT. C-PSE = combination prophylactic swallowing exercise group; ID-PSE = indirect PSE group; PEG = percutaneous endoscopic gastrostomy; RT = radiotherapy

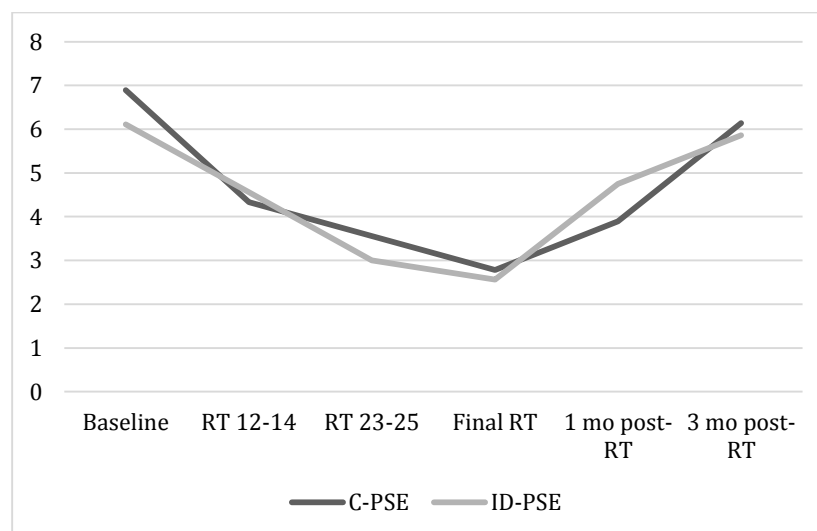


Figure 5. Mean FOIS scores from baseline to three months post-RT/CRT. C-PSE = combination prophylactic swallowing exercise group; ID-PSE = indirect PSE group; FOIS = Functional Oral Intake Scale; mo = month; RT = radiotherapy

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In addition to PEG-use rates, patients who were dependent on a PEG-tube at the final RT/CRT session were asked to provide the first date they no longer required the use of the PEG-tube for nutritional supplement. In some instances, patients were not able to recall the exact date, but were able to give an approximation. Enough data was obtained to determine PEG-discontinuation rates at one month, two months, and three months post-RT/CRT. PEG-discontinuation rates were used rather than PEG-discharge rates because the time between discontinuation of PEG use and PEG discharge varied greatly across patients. For instance, one patient in the ID-PSE group indicated that she stopped using her PEG-tube over three months before she had it removed. PEG-discontinuation rate was, therefore, thought to be a more accurate representation of PEG dependence than PEG-discharge rate.

Six of nine patients (66%) in the C-PSE group and eight of nine patients (89%) in the ID-PSE group were using a PEG tube at the final RT/CRT session. Of these patients, data was missing for one patient in the C-PSE group at two and three months post-RT/CRT and for one patient in the ID-PSE group at one month post-RT/CRT. By one month post, 50% (3/6) of the C-PSE patients and 29% (2/7) of the ID-PSE patients had discontinued using their PEG tube. By two months post, 80% (4/5) of the C-PSE patients accounted for, and 63% (5/8) of the ID-PSE patients had discontinued using the PEG-tube. This rate did not change at three months post-RT/CRT for the C-PSE patients, but improved to 88% (7/8) for the ID-PSE patients. Table 12 and Figure 6 provides these descriptive statistics. Significance tests using the Fisher's exact test did not reveal any significant between-group differences at one month post-RT/CRT ($p = .296$), two months post-RT/CRT ($p = .50$), or three month post-RT/CRT ($p = .50$).

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Table 12

PEG-tube discontinuation rates at the end of RT, one month post-RT, two months post-RT/CRT, and three months post-RT/CRT. P-value by Fisher's Exact test

	C-PSE Group		ID-PSE Group		Total		p-value
	N	PEG d/c rate (%)	N	PEG d/c rate (%)	N	PEG d/c rate (%)	
Final-RT	6	0	8	0	14	0	NA
1-mo post RT	6	.50	7	.29	13	.40	.296
2-mo post RT	5	.80	8	.63	13	.72	.50
3-mo post RT	5	.80	8	.88	13	.84	.50

Note. d/c = discontinuation; PEG = percutaneous endoscopic gastrostomy; mo = month; RT = radiotherapy

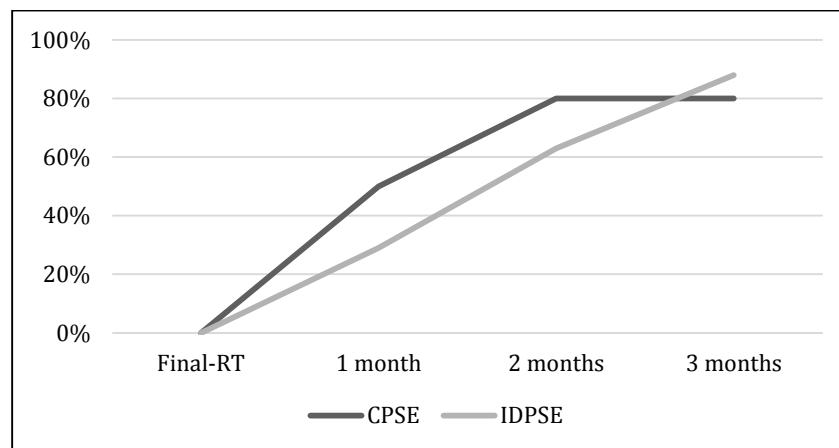


Figure 6. Percent of patients who discontinued PEG-tube use at the final-RT, one month, two months, and three months, post-RT/CRT.

Swallowing Function

Swallowing function was measured with the Eating Assessment Tool-20 (EAT-20) and the MD Anderson Dysphagia Inventory (MDADI). As explained in Chapter 3 of this dissertation, the MDADI was added late in the data collection process and so was not collected on the first six patients.

Eating Assessment Tool-20 (EAT-20). As described in the Measures section of Chapter 3, the EAT-20 scores were divided into *physical*, *emotional*, and *functional* subscales modeled after the MDADI. Higher scores on the EAT-20 indicated worse self-perceived swallowing function.

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As expected, EAT-20 scores increased progressively in both groups during RT/CRT and then gradually declined during the post-RT/CRT phase. Scores were similar between both groups at each point during the treatment phase of the study as can be seen in Figure 7. At one month post-RT/CRT, EAT-20 scores were higher in the C-PSE group than the ID-PSE group. One month post scores for the C-PSE group and ID-PSE group respectively were as follows: EAT-20-*Total*: 31.67 vs. 16.88, EAT-20-P: 17.44 vs. 3.87, EAT-20-F: 6.11 vs. 3.87, and EAT-20-E: 8.11 vs. 5.25. At three months the pattern reversed and favored the C-PSE group on all EAT-20 scores except for the EAT-20-F score. Scores at three months post-RT/CRT for the C-PSE and ID-PSE groups respectively were as follows: EAT-20-*Total*: 6.14 vs. 13.86, EAT-20-P: 2.71 vs. 7.43, EAT-20-F: 2.00 vs. 2.00, and EAT-20-E: 1.43 vs. 4.43. This reversal pattern that favored the C-PSE group at three months post-RT/CRT was exclusively due to patient 13 of the ID-PSE group, who was the only patient in both groups whose scores actually worsened from one month post to three months post. As can be seen in Figures 9, 11, and 13, when patient 13 was excluded from the data, EAT-20 means for the ID-PSE group were relatively equivalent or lower than the C-PSE means at three months post-RT/CRT. All mean EAT-20 scores in the post-treatment phase are included in Table 13.

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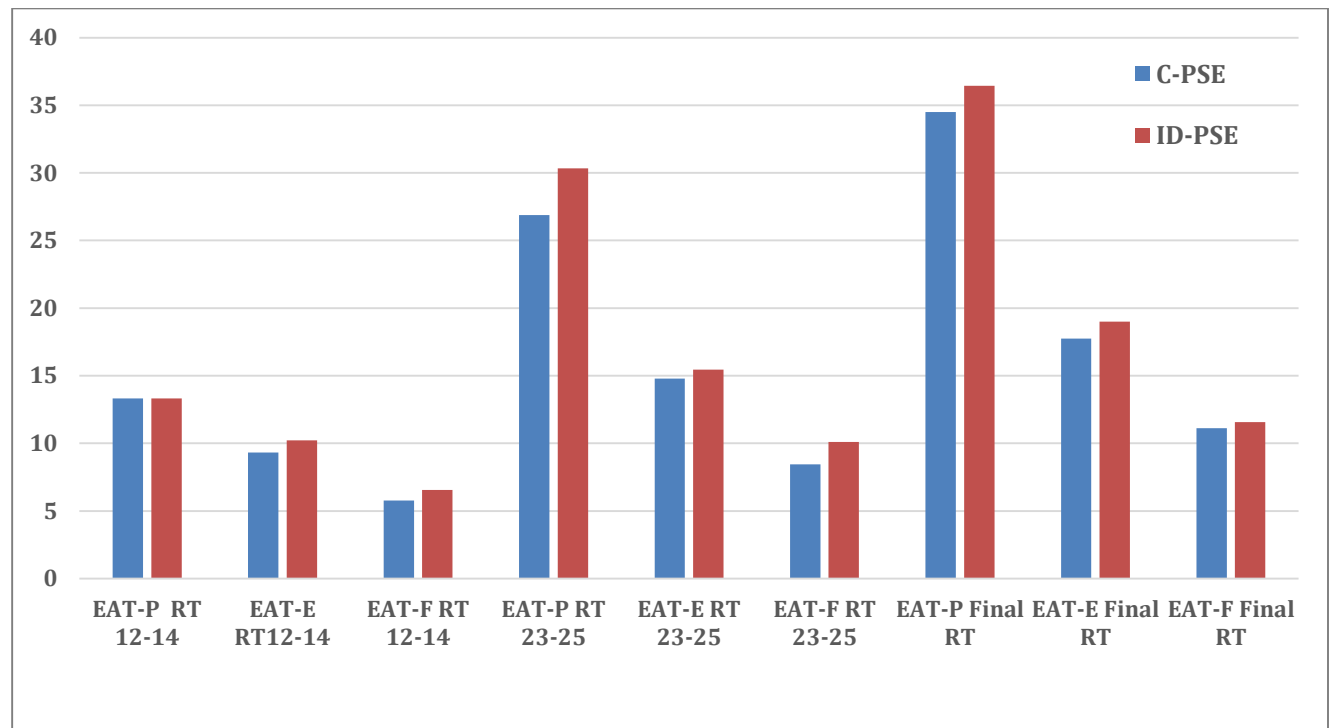


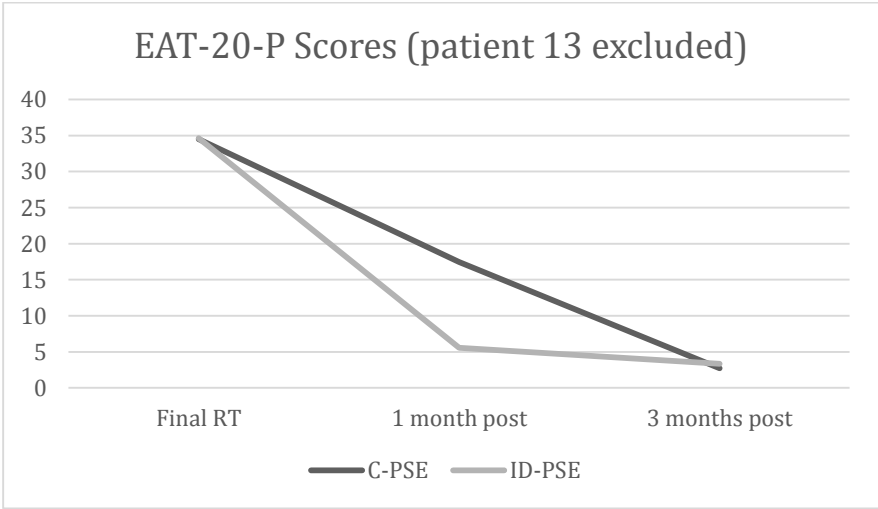
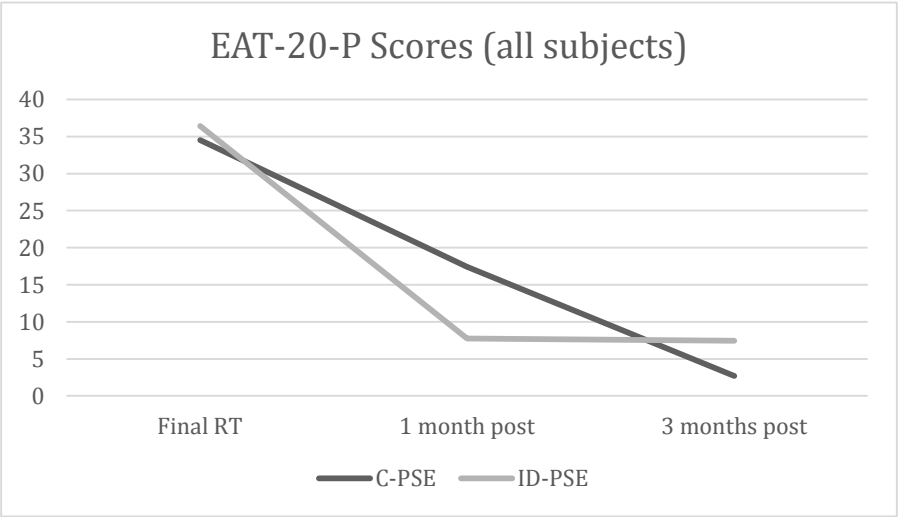
Figure 7. Mean EAT-20 subscale scores during RT/CRT. EAT = Eating Assessment Tool; E = emotional subscale; F = functional subscale; P = physical subscale.

Table 13

Mean EAT-20-Total and EAT-20 subscale scores at the end of RT/CRT and during the post-RT/CRT phase. Standard deviations in parentheses

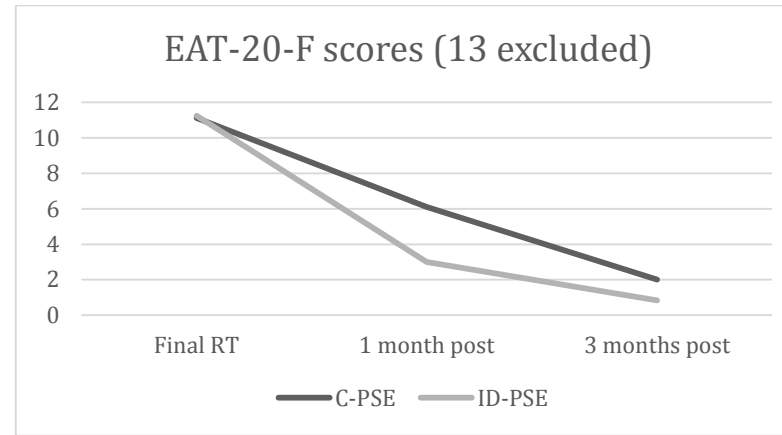
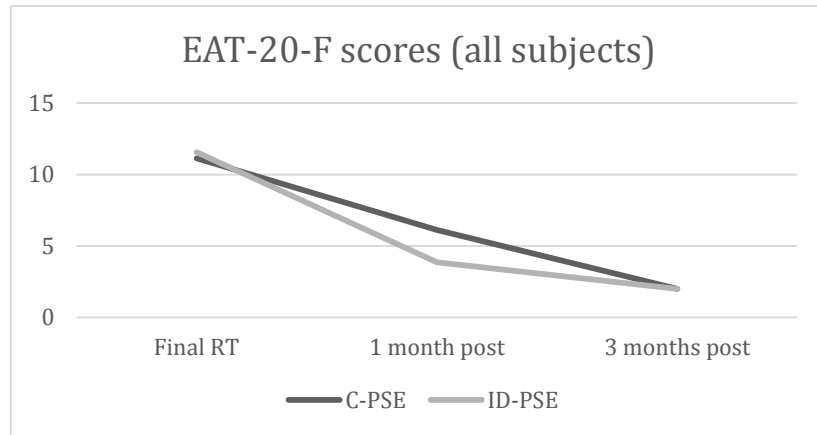
	EAT- 20-Total	Final RT session			EAT- 20-Total	1 month post-RT/CRT			EAT- 20-Total	3 months post-RT/CRT		
		EAT- 20-P	EAT- 20-F	EAT- 20-E		EAT- 20-P	EAT- 20-F	EAT- 20-E		EAT- 20-P	EAT- 20-F	EAT- 20-E
C-PSE Group	63.38 (34.41)	34.5 (20.84)	11.13 (4.16)	17.75 (11.47)	31.67 (35.13)	17.44 (21.80)	6.11 (5.84)	8.11 (9.18)	6.14 (7.53)	2.71 (2.81)	2.00 (4.00)	1.43 (1.81)
ID-PSE Group	67.00 (27.34)	36.44 (16.43)	11.56 (3.88)	19.00 (9.15)	16.88 (18.07)	7.75 (7.83)	3.87 (3.98)	5.25 (6.58)	13.86 (21.64)	7.43 (11.09)	2.00 (3.41)	4.43 (7.44)

Note. EAT = Eating Assessment Tool; E = Emotional subscale; F = Functional subscale P = Physical subscale; RT = radiotherapy; CRT = chemoradiotherapy

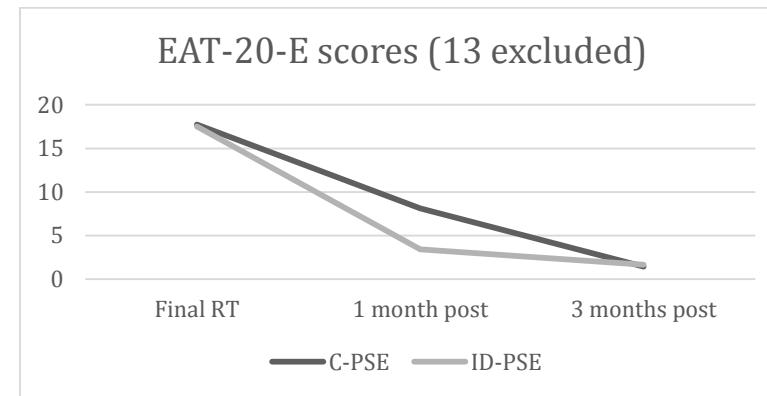
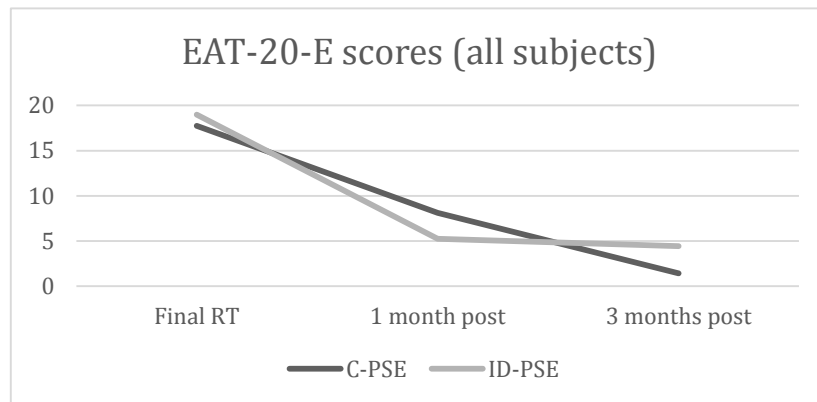


Figures 8 and 9. Mean EAT-20-P scores during the post-RT/CRT phase with patient 13 (left) and with patient 13 excluded (right).

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Figures 10 and 11. Mean EAT-20-F scores during the post-RT/CRT phase with patient 13 (left) and with patient 13 excluded (right).



Figures 12 and 13. Mean EAT-20-E scores during the post-RT/CRT phase with patient 13 (left) and with patient 13 excluded (right).

To analyze between-group differences in the post-RT/CRT phase, difference scores were calculated for each patient by subtracting the one month and three month post-RT/CRT EAT-20 scores from the final-RT EAT-20 scores. Analysis of between-group differences on the difference scores using the Mann-Whitney U test revealed a significant difference in the EAT-20-*Total* difference scores for one month post-RT/CRT ($U = 49, z = 1.79, p = .042, r = .45$) indicating that overall patients in the ID-PSE group had better self-perceived swallowing function at one month post-RT/CRT than patients in the C-PSE group. Difference scores on the EAT-20-P ($U = 47, z = 1.58, p = .065, r = .39$) approached significance. There were no significant differences in EAT-20-E ($U = 42.5, p = .14$) or EAT-20-F ($U = 45, p = .10$) one month difference scores. To determine if the lack of significance on the EAT-20-P, EAT-20-E, and EAT-20-F one month difference scores was due to patient 13, the same analyses were completed with patient 13's data excluded. Excluding patient 13 did not result in any significant between-group differences and minimal changes in significance levels. There were no significant between-group differences for three months post-RT/CRT difference scores (all patients included). Mean one month and three month difference scores are catalogued in Table 14. Mean ranks and significance test results are catalogued in Table 15.

Table 14

Mean difference scores on the EAT-20 subscales at one month post-RT/CRT and three months post-RT/CRT. Difference scores calculated by subtracting one and three month post-RT/CRT scores from the final-RT scores. Standard deviations in parentheses

	<u>C-PSE Group</u>			<u>ID-PSE Group</u>		
	N	Diff. score	Range	N	Diff. score	Range
EAT-20-Total						
1 month post	8	28.00 (22.44)	1-64	8	47.63 (24.37)	14-81
3 months post	6	54.00 (33.67)	7-109	7	51.00 (28.99)	14-84
EAT-2- <i>Emotional</i>						
1 month post	8	8.63 (8.62)	0-25	8	13.00 (8.97)	3-26
3 month post	6	16.33 (11.15)	3-37	7	12.57 (8.16)	3-24
EAT-20- <i>Functional</i>						
1 month post	8	4.38 (4.96)	-1-14	7	7.25 (4.06)	1-12

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3 month post	6	7.67 (6.06)	-1-15	7	8.86 (4.81)	1-13
EAT-20-Physical						
1 month post	8	15.00 (16.96)	2-57	8	27.38 (15.27)	10-49
3 month post	6	30.00 (20.91)	2-57	7	29.57 (16.87)	9-51

Note. Diff = difference

Table 15

Mean ranks for EAT-20 subscale difference scores at one month post-RT/CRT and three months post-RT/CRT. Z-score, p-value, and effect sizes determined by Mann-Whitney U test

	C-PSE Group		ID-PSE Group		z-score	U	p-value (1-tailed)	Effect size (r)
	N	Mean Rank	N	Mean Rank				
EAT-20-Total								
1 month post	8	6.38	8	10.62	1.79	49.00	.04*	.45
3 month-post	6	7.00	7	7.00	0	21.00	.50	0
EAT-20-E								
1 month-post	8	7.19	8	9.81	1.10	42.50	.14	.28
3 month-post	6	7.42	7	6.64	-.360	18.50	.37	-.09
EAT-20F								
1 month-post	8	6.88	8	10.12	1.38	45.00	.10	.35
3 month-post	6	6.50	7	7.43	.432	24.00	.37	.12
EAT-20-P								
1 month-post	8	6.62	8	10.38	1.58	47.00	.065	.40
3 month-post	6	7.08	7	6.93	-.072	20.50	.47	-.02

Note. CRT = chemoradiotherapy; NA = not applicable, MDADI = MD Anderson Dysphagia Inventory; RT = radiotherapy

*Significant at alpha level = .05

MD Anderson Dysphagia Inventory (MDADI). MDADI scores were only available for four C-PSE patients and six ID-PSE patients at the final-RT/CRT time point, five C-PSE patients and seven ID-PSE patients at one month post, and four C-PSE and seven ID-PSE patients at three months post. The MDADI is scored according to *global* (MDADI-G), *emotional* (MDADI-E), *functional* (MDADI-F), and *physical* (MDADI-P) subscales. Subscale sums are transformed to a 0-100 point scale with 0 being the worst functioning and 100 being the best functioning. Mean MDADI subscale scores for the C-PSE and ID-PSE groups at the final RT/CRT session were:

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global 30 vs. 60, *emotional* 55.83 vs. 78.89, *functional* 66 vs. 72.67, and *physical* 52.50 vs. 58.33, respectively. Between-group differences in MDADI scores at the final RT session were analyzed with the Mann-Whitney U test, which revealed insignificant differences in the MDADI-F ($U = 15, p = .305$) and MDADI-P ($U = 14, p = .381$) subscales, but a significant difference on the MDADI-E subscale ($U = 21, z = 1.92, p = .034, r = .61$) and a near significant difference on the MDADI-G ($U = 20, z = 1.92, p = .057, r = .61$). This indicated that the ID-PSE group had better swallowing related emotional QOL and probable better global swallowing-related QOL at the end of RT/CRT than the C-PSE group. Mean MDADI scores at the end of RT/CRT are shown in Figure 14 and Table 16. Table 17 summarizes mean ranks and test statistics.

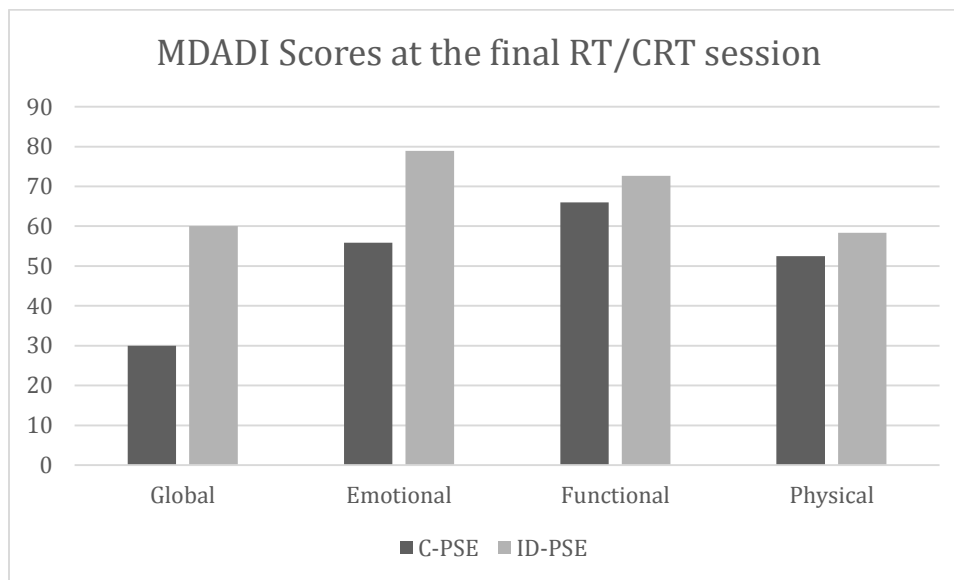


Figure 14. MDADI scores at the final RT/CRT session. MDADI = MD Anderson Dysphagia Inventory

Mean MDADI scores for the C-PSE and ID-PSE groups at one month post-RT/CRT favored the ID-PSE group and were as follows: *global* 64.00 vs. 77.14, *emotional* 64.67 vs. 86.67, *functional* 54.40 vs. 83.43, and *physical* 55.50 vs. 71.07, respectively. At three months post-

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RT/CRT MDADI scores on all subscales were very similar between the two groups with mean *global* scores of 95.00 vs. 82.86, mean *emotional* scores of 95.00 vs. 92.86, mean *functional* scores of 92.00 vs. 91.43, and mean *physical* scores of 76.88 vs. 72.86, respectively. These scores are summarized in Table 16 and Figures 15-18.

Table 16

Mean MDADI scores at the final-RT session, one month post-RT/CRT, and three months post-RT/CRT. Standard deviations in parentheses

	C-PSE Group						ID-PSE Group					
	Final-RT		1-mo post		3-mo post		Final-RT		1-mo post		3-mo post	
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
MDADI-G	4	30 (11.55)	5	64.00 (32.86)	4	95.00 (10.00)	6	60.00 (30.98)	7	77.14 (17.99)	7	82.86 (29.28)
MDADI-E	4	55.83 (11.34)	5	64.67 (11.45)	4	95.00 (4.30)	6	78.89 (18.82)	7	86.67 (13.19)	7	92.86 (8.48)
MDADI-F	4	66.00 (12.44)	5	54.40 (11.52)	4	92.00 (13.47)	6	72.67 (12.24)	7	83.43 (9.91)	7	91.43 (13.55)
MDADI-P	4	52.50 (12.42)	5	55.50 (5.42)	4	76.88 (12.81)	6	58.33 (8.16)	7	71.07 (13.53)	7	72.86 (19.06)

Note. CRT = chemoradiotherapy; E = emotional; F = functional; G = global; MDADI = MD Anderson Dysphagia Inventory; mo = month; P = physical

Due to missing data, difference scores were only obtainable for three patients in the C-PSE group and six patients in the ID-PSE group. Between-group differences in the post-RT/CRT phase were therefore, tested on the raw scores using the Mann-Whitney U test. Visual inspection of the data showed no significant differences between the two groups at three months post-RT/CRT, but there was a pattern of better MDADI scores in the ID-PSE group than the C-PSE group on all of the MDADI subscales at one month post-RT/CRT (Figures 16-196). The Mann-Whitney U test confirmed this difference to be significant for the MDADI-E ($U = 31.5$, $z = 2.29$,

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$p = .009$, $r = .66$), the MDADI-F ($U = 35$, $z = 2.85$, $p = .002$, $r = .82$), and the MDADI-P ($U = 31$, $z = 2.20$, $p = .015$, $r = .64$), each of which had large to very large effects sizes. There was no significant difference in MDADI-G scores ($U = 21$, $p = .320$). Mean ranks for the MDADI during the post-RT/CRT phase are presented in Table 17.

In summary, the evidence indicates that patients in the ID-PSE group improved swallowing function more rapidly in the first month following RT/CRT than patients in the C-PSE group. By three months post, this difference between the groups was no longer evident, indicating that the C-PSE group had caught up to the ID-PSE group regarding swallowing function.

Table 17

Mean ranks for MDADI subscale scores at the final-RT session, one month post-RT/CRT, and three months post-RT/CRT. Z-score, p-value, and effect size determined by Mann-Whitney U test

	C-PSE Group		ID-PSE Group		z-score	U	p-value (1-tailed)	Effect size (r)
	N	Mean Rank	N	Mean Rank				
MDADI-Global								
Final-RT	4	3.50	6	6.83	1.94	20.00	.057	.61
1 month-post	5	3.80	7	8.83	2.20	21.00	.312	.64
3 month-post	4	6.75	7	5.57	-.665	11.00	.324	-.20
MDADI-Emo.								
Final-RT	4	3.25	6	7.00	1.92	21.00	.034*	.61
1 month-post	5	3.70	7	8.50	2.29	31.50	.009*	.66
3 month-post	4	6.12	7	5.93	-.097	13.50	.463	-.03
MDADI-Funct.								
Final-RT	4	4.75	6	6.00	.644	15.00	.305	.20
1 month-post	5	3.00	7	9.00	2.85	35.00	.002*	.82
3 month-post	4	5.88	7	6.07	.103	14.50	.50	.03
MDADI-Physical								
Final-RT	4	5.00	6	5.83	.430	15.00	.381	.14
1 month-post	5	3.80	7	8.43	2.20	31.00	.015*	.64
3 month-post	4	6.25	7	5.86	-.189	13.00	.463	-.06

Note. NA = not applicable, MDADI = MD Anderson Dysphagia Inventory; RT = radiotherapy

*Significant at alpha level = .05

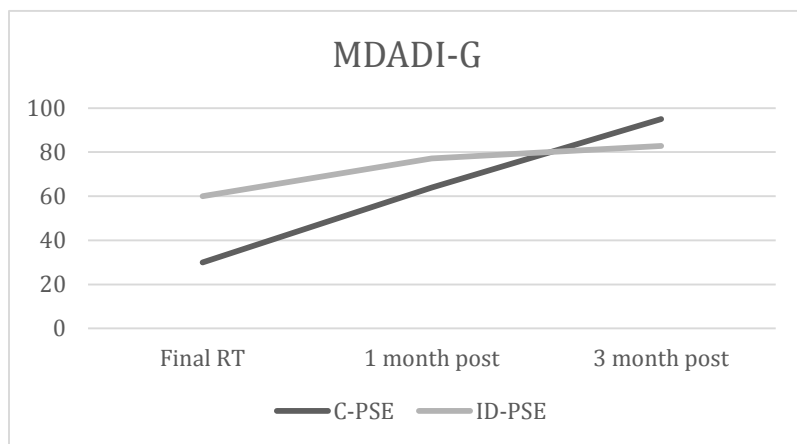


Figure 15. Mean MDADI-Global post-RT/CRT scores

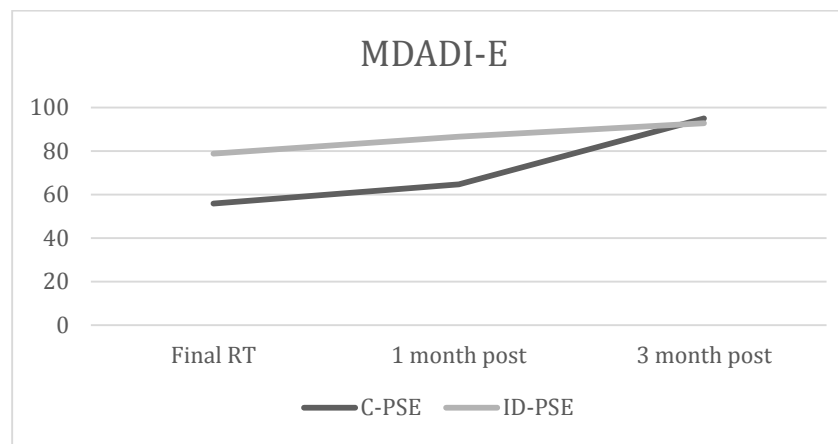


Figure 16. Mean MDADI-Emotional post-RT/CRT scores

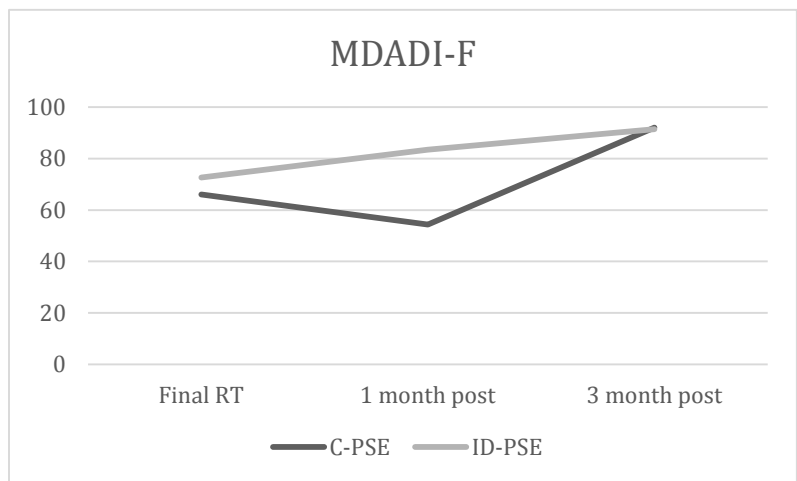


Figure 17. Mean MDADI-Functional post-RT/CRT scores

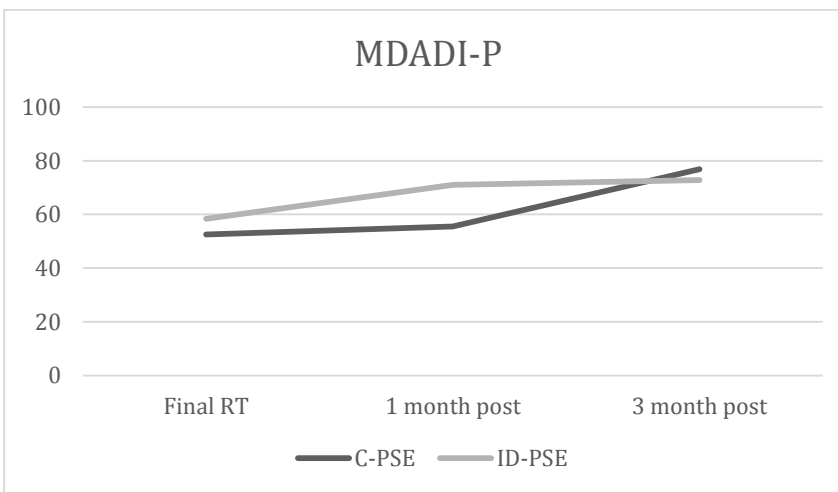


Figure 18. Mean MDADI-Physical post-RT/CRT scores

Swallowing Pain. Swallowing pain was measured on a scale from 0 (i.e., no pain) to 5 (i.e., excruciating pain). Mean pain rating increased relatively steadily throughout RT/CRT and gradually declined during the post-RT/CRT phase for both groups. Mean pain during RT/CRT for the C-PSE and ID-PSE groups were 1.67 vs. 1.78 at RT 12-14, 2.22 vs. 1.89 at RT 23-25, and 1.89 vs. 2.44 on the last day of RT, respectively. During the post-RT/CRT phase, mean pain scores for the C-PSE and ID-PSE groups were .89 vs. .88 at one month post-RT/CRT and .14 vs. 1.00 at three months post-RT/CRT, respectively. Visual inspection of the data (Figure 19) indicated a potential significant difference between the groups at the final-RT session and three months post-RT/CRT, both favoring the C-PSE group. Mann-Whitney U test on the raw scores failed to show a significant difference between the groups for the last day of RT ($U = 51.5, p = .17$), but confirmed a significant difference at three months post-RT/CRT ($U = 39, z = 2.109, p = .037, r = .56$). Contrary to our hypothesis, this indicates that swallowing pain was actually worse in the ID-PSE group than the C-PSE group. However, it is relevant to note that patient 13 was again an outlier in the ID-PSE group, and as such, contributed to this difference. At three months post-RT/CRT patient 13 had a pain score of 3, while everyone else in the ID-PSE group as well as the C-PSE group had a pain score of 0 or 1. With patient 13 removed from the data, the difference between the groups approached but was not significant ($U = 32, p = .07$). Mean ranks and significance levels (patient 13 included) are presented in Table 18.

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Table 18

Mean swallowing-pain scores, standard deviations, ranges, and mean ranks at RT 12-14, RT 23-25, Final RT, one month post-RT/CRT, and three months post-RT/CRT. Pain scores based on 0-5 scale (i.e., 0 = no pain, 1 = mild pain, 2 = moderate pain, 3 = moderate to severe pain, 4 = severe pain, 5 = excruciating pain)

	C-PSE				ID-PSE						
	N	Mean Pain (SD)	Range	Mean Rank	N	Mean Pain (SD)	Range	Mean Rank	z-score	p-value (1-tailed)	Effect size (r)
RT 12-14	9	1.67 (1.11)	0-3	9.61	9	1.78 (1.09)	1-4	9.39	-.092	.466	-.02
RT 23-25	9	2.22 (1.64)	0-4	10.06	9	1.89 (1.36)	0-4	8.94	-.454	.333	-.12
Final RT	9	1.89 (1.36)	0-4	8.28	9	2.44 (1.13)	1-4	10.72	1.01	.170	.24
1 month post	9	.89 (.93)	0-3	8.72	8	.88 (.64)	0-2	9.31	.274	.408	.07
3 month post	7	.14 (.38)	0-1	5.43	7	1.00 (1.00)	0-3	9.57	2.109	.037*	.56

Note. CRT = chemoradiotherapy; RT = radiotherapy; SD = standard deviation

*Significant at alpha = .05

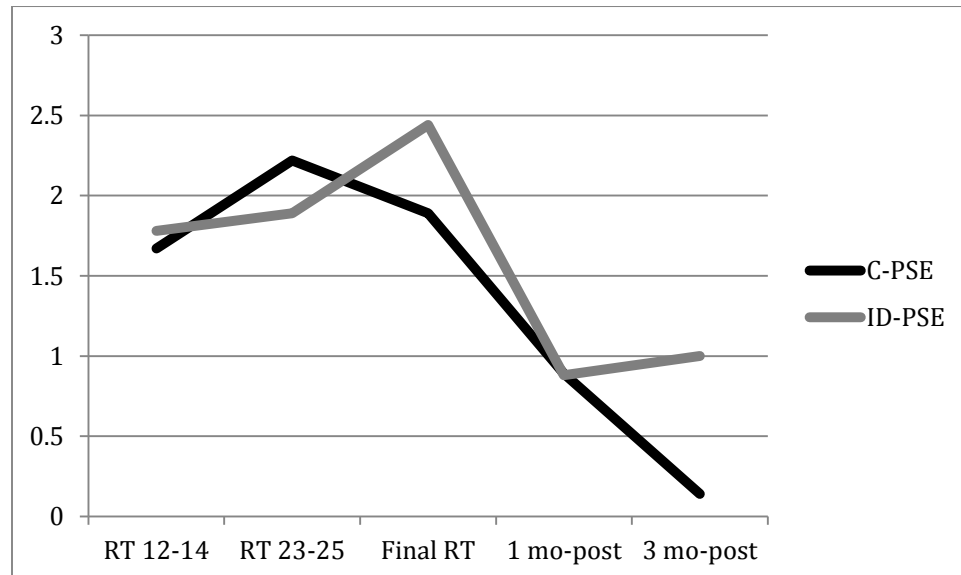


Figure 19. Mean swallowing pain scores per group at RT 12-14, RT 23-25, final-RT, one month post-RT/CRT, and three months post-RT/CRT. *mo* = month, *RT* = radiotherapy

Chapter 5: Discussion

The purpose of this study was to contribute to the evidence-base of prophylactic care for patients with RT/CRT-toxicity-induced dysphagia secondary to HNC. The study sought to investigate the efficacy of a prophylactic swallowing exercise (PSE) program involving solely indirect swallowing exercises (ID-PSE) for the purpose of creating an effective PSE program that is more comfortable for patients, improves compliance, and maximizes swallowing function. The ID-PSE program was compared to a more traditional PSE program that consisted of a combination of direct and indirect swallowing exercises (C-PSE).

Alternate assignment was used to place eighteen patients in either the C-PSE ($n = 9$) or ID-PSE ($n = 9$) group. Patients in both groups began their exercises within two weeks of beginning RT/CRT and were encouraged to continue the exercises throughout RT/CRT. Patients in the C-PSE group were prescribed the effortful swallow, Mendelsohn maneuver, Masako maneuver, and the Shaker exercise. Patients in the ID-PSE group were prescribed the Shaker, pharyngeal squeeze, tongue-base retraction, and lingual and jaw range-of-motion exercises. All exercises were completed three times per day (see the Methods section for exact dose per exercise session for each exercise). Outcome measures, including the Eating Assessment Tool (EAT-20), Functional Oral Intake Scale (FOIS), percent PEG-tube use, MD Anderson Dysphagia Inventory (MDADI), and swallowing pain, were collected at baseline, three times during RT/CRT, and at one month and three months post-RT/CRT. There were no statistically significant differences between the groups in baseline outcome measures, demographics, cancer characteristics, or cancer treatment. We hypothesized that the ID-PSE program would minimize swallowing pain and subsequently would result in improved PSE compliance, improved oral intake, improved swallowing function, and less swallowing pain relative to the C-PSE group.

Compliance

We hypothesized that patients in the ID-PSE group would be more compliant to their PSE program than patients in the C-PSE group because the ID-PSE program would be more comfortable due to not having to swallow during the exercises. Although compliance in the ID-PSE group was higher than in the C-PSE group during the pre-RT phase and for the first four weeks of RT/CRT, the difference was not statistically significant. The hypothesis, therefore, was not confirmed. Both groups were between 40-50% compliant overall and both groups generally declined in compliance throughout RT/CRT.

The pattern of gradual decline in compliance throughout RT/CRT is consistent with all other PSE studies that report on compliance (Carnaby-Mann et al., 2011; Kotz et al., 2012; van der Molen et al., 2011; Virani et al., 2015). Overall rate of compliance was consistent van der Molen et al. (2011), who also reported an average compliance of around 40%. Carnaby-Mann et al. (2011), however, reported average compliance of 68% overall. The factor that may have contributed to Carnaby-Mann et al.'s improved compliance relative to the current study was frequency of meetings with a speech-language pathologist (SLP). Carnaby-Mann et al. reported that a research SLP met with patients twice daily throughout the first six weeks of CRT to complete swallowing exercises. In the current study patients were relied upon to complete their swallowing exercises independently at home; an SLP only met with patients three times during RT/CRT to collect data. This is consistent with literature that indicates that supervised exercise programs result in better compliance and better outcomes than unsupervised exercise programs (Koh, Saxena, Ng, Yong, & Fong, 2012; Olney et al., 2006; Sluijs et al., 1993).

Additional factors discussed in the literature regarding exercise compliance that may have played a role in compliance in the current study include patients' belief and perception of the potential

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benefit of the exercise (Sluijs et al., 1993), and generally feeling ill (Cohen-Mansfield, Marx, & Guralnik, 2003). It may be that patients in the C-PSE group had a greater belief in the benefit of their PSE program than patients in the ID-PSE group. This makes sense given that during the training phase of the study the importance of swallowing was emphasized to all patients and one explanation of decreased swallowing function during RT/CRT was a reduction or avoidance of swallowing. Further, it may simply be that generally feeling fatigued and sick outweighed any other factors impacting compliance, which is consistent with literature indicating that the single greatest predictor of exercises compliance in the elderly is health and pain (Cohen-Mansfield et al., 2003).

Lastly, it may be that the ID-PSE program was in fact not more comfortable than the C-PSE program. In hindsight, it would have been prudent to ask patients a specific question about comfort level with the PSE program rather than only asking about pain with swallowing. Anecdotally, some patients in the ID-PSE group did report that towards the end of RT/CRT completing the exercises was painful. It is likely that mucositis-related pain is severe enough that not only swallowing, but also simply moving oral and pharyngeal structures is painful.

Oral Intake

The second hypothesis of the study was that patients in the ID-PSE group would have better oral intake outcomes than patients in the C-PSE group. Oral intake outcomes were measured with percent PEG-tube use, the FOIS, and PEG-tube discontinuation rates. The data failed to support the hypothesis. There were no significant differences in any oral intake outcomes between the two groups at any time point.

Functional Oral Intake Scale. Outcomes on the FOIS were consistent with several prior PSE studies. Carnaby-Mann et al. (2011), van der Molen et al. (2011), and Virani et al. (2015) all also found no differences in FOIS scores between different types of PSE. This may indicate that the FOIS is

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not sufficiently sensitive to detect differences in oral intake, particularly given that each of these authors found significant differences between treatment groups on other outcome measures. In the current study, mean FOIS score for both groups combined was 4.29 at one month post-RT/CRT (median = 4) and 6 at three months post-RT/CRT (median = 6.5). These rates are comparable to van der Molen et al. (2011), who reported a mean FOIS of 5 at 10 weeks post-RT in patients completing PSE and Kotz et al. (2012), who reported a median FOIS of 7 at three months post-RT in patients complete PSE.

PEG-tube dependence. PEG-tube dependence rates were also comparable to other PSE studies. In the current study, overall PEG-tube dependence at three months post-RT/CRT was equivalent across the two groups at 12% (1/8) for each group. This rate was slightly better than Virani et al. (2015), who reported a PEG-dependence rate of 16% at three months post-RT/CRT in patients completing several PSEs. Further, Virani et al.'s comparison group, who's PSE consisted of repetitive swallowing, had a PEG-dependence rate of 50% at three months post-RT/CRT, which is much worse than the current study's rate of 12%. Additionally, the current study's PEG-dependence rate of 12% at three months post is much better than the typical rate of 50% or higher in patients who do not complete any PSEs (Greven et al., 2008; Logemann et al., 2008).

In summary, although the current study did not find evidence of a difference in oral intake outcomes between the two treatment groups, results of both groups are comparable to other PSE studies and better than patients who do not complete PSEs. This is an indication that both PSE programs were effective in regards to improving oral intake outcomes relative to previous studies.

Swallowing Function

In regards to swallowing function, we hypothesized that patients in the ID-PSE group would report better swallowing function than patients in the C-PSE group. This hypothesis was tested using

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two self-reported swallowing-function outcome measures – the Eating Assessment Tool (EAT-20) and the MD Anderson Dysphagia Inventory (MDADI). Both tools were divided into *emotional*, *functional*, and *physical* subscales. The MDADI also included a *global* subscale and the EAT-20 also included a total score.

Although between-group differences were not evident on every subscale of either the EAT-20 or the MDADI, the ID-PSE group had significantly better scores on four (i.e., EAT-20-Total, MDADI-E, MDADI-F, and MDADI-P) of the eight total subscales at one month post-RT/CRT, and scores on the EAT-20-P approached significance ($p = .065$). This evidence is an indication that patients in the ID-PSE group recovered swallowing function faster in the first month post-RT/CRT than patients in the C-PSE group, which supports the hypothesis. This is the first PSE study to show a difference in outcomes as early as one month post-RT/CRT. Other PSE studies do not show a difference between groups until three months post-RT/CRT or later (Carnaby-Mann et al., 2011; Carroll et al., 2008; Kotz et al., 2012; van der Molen et al., 2011; Virani et al., 2015).

No prior PSE studies included the EAT-20, preventing cross-study comparison on that measure. However, two prior PSE studies included the MDADI. Virani et al. (2012) reported MDADI scores on HNC patients immediately post-RT/CRT. MDADI scores on the last day of RT in the current study were very similar to Virani et al.'s post-RT/CRT scores with *global* mean scores of 48 vs. 42, *emotional* mean scores of 69.7 vs. 72.3, *functional* mean scores of 70 vs. 64, and *physical* mean scores of 56 vs. 55.3, respectively. Kulbersh et al.'s (2006) MDADI scores were obtained six to 12 months following RT/CRT. Those scores (*global*: 71.6, *emotional*: 71.5, *functional*: 68.3, and *physical*: 48.8) were slightly lower than the overall mean MDADI scores at three months post-RT/CRT in the current study (*global*: 87.3, *emotional*: 93.6, *functional*: 91.6, *physical*: 74.3), indicating that patients in the

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current study had better self-perceived swallowing function at three months post-RT/CRT than patients in the Kulbersh et al.'s study had at one year post-RT/CRT.

In comparison to literature that includes MDADI outcomes in HNC patients who did not receive PSE, the current study showed favorable results. Gillespie, Brodsky, Day, Lee, and Martin-Harris (2004) reported MDADI scores on patients treated with CRT for oropharyngeal cancer at 12 months post-CRT. Their scores were slightly lower than MDADI scores in the current study at three months post-RT/CRT with MDADI *global* scores of 80 vs. 87.3, *emotional* scores of 76.8 vs. 93.6, *functional* scores of 86.4 vs. 91.6, and *physical* scores of 64.5 vs. 74.3, respectively.

Overall, patients in the current cohort had better self-perceived swallowing function as measured by the MDADI than patients in both Kulbersh et al. (2006) and Gillespie et al. (2004); however, these are not entirely fair comparisons given that by 12 months post-RT/CRT patients in both Kulbersh et al. and Gillespie et al.'s study may have developed worsening dysphagia due to late-effects of RT/CRT.

Swallowing Pain

We hypothesized that patients in the ID-PSE group would report less swallowing pain than patients in the C-PSE group because patients in the ID-PSE group did not have to swallow during their PSEs. The analysis of the data, however, indicated that the only difference in swallowing pain between the two groups was at three months post-RT/CRT, at which point the ID-PSE group actually had more swallowing pain than the C-PSE group. We suspected that this statistical difference was primarily due to patient 13 who was an outlier in the ID-PSE group; however, removing patient 13 only slightly increased the *p*-value above the significance level (i.e., .07). Explaining this difference between the two groups is difficult. Further study is necessary to ensure this is a valid finding and to explore potential reasons for the difference between the two groups. As discussed above, since the purpose of designing

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a PSE program consisting solely of indirect swallowing exercises was to make the program more comfortable, it would have been more telling to ask patients to rate their comfort level while performing the PSEs, rather than rating swallowing pain in general. The lack of between-group differences in swallowing pain was likely due to the severity of pain caused by mucositis outweighing any additional impact of the PSEs on swallowing pain.

Relative to the literature, swallowing pain in the current study was comparable to van der Molen et al. (2011) who reported that 45% of patients had no swallowing pain at 10 weeks post-CRT. In the current study, 29% of patients overall had no pain at four weeks post-RT/CRT and 57% had no pain at three months post-RT/CRT.

Limitations

Several limitations to this study should be considered when determining the strength of the conclusions drawn from the study. These limitations included a small sample size, the lack of a no-treatment control group, the late addition of the MDADI, and the lack of an instrumental swallowing evaluation during the post-RT/CRT phase to objectively assess swallowing function. Additionally, the inclusion criteria, and what data and how the data was collected, had inherent limitations.

The limitation in sample size is a common challenge when doing human-subject research on disordered populations, particularly in relatively rural communities such as Missoula, MT. The small number of patients in each group certainly negatively impacted the statistical power of the analysis and the subsequent confidence regarding the results. Impacting this issue further was the late addition of the MDADI and attrition, both of which contributed to even lower sample sizes in the post-RT/CRT phase. The trend favoring the ID-PSE group provides a strong rationale for continuation of this project; however, expansion of the current study, as well as replication of the results are necessary before firm conclusions can be made.

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The lack of a post-RT/CRT instrumental swallowing assessment limits the confidence in conclusions made regarding post-RT/CRT swallowing function; however, there were several reasons for not including an instrumental swallowing study post-RT/CRT. First, HNC patients have been treated in this region for numerous years without regular post-RT/CRT instrumental swallowing assessments and without any clear negative outcomes as a result. It was, therefore, difficult to argue the need for an instrumental assessment for every patient unless that assessment could be provided free-of-charge, which was not feasible, given that it would not have been possible for the principle investigator to conduct all instrumental studies, due to some patients not tolerating a FEES exam. Additionally, having multiple SLPs conducting the instrumental studies would have reduced the reliability of the results. The MBS in particular has been shown to have poor inter-rater reliability (Stoeckli, Huisman, Seifert, & Martin-Harris, 2003; Wilcox, Liss, & Siegel, 1996).

In hindsight, it may have been warranted to include in the inclusion criteria that all patients have functional swallowing ability at baseline to meet 100% of their nutritional needs. Intuitively, this makes sense given that the overarching topic of this research is prophylactic intervention and prescribing swallowing exercises for patients who already have severe dysphagia would not be considered prophylactic. Fortunately, only one patient in the study started with severe dysphagia, and although she was an outlier within the ID-PSE group, her scores did not appear to have a significant impact on the analysis. However, additional patients with non-functional swallowing at baseline may have a significant impact on our ability to infer results for patients who begin with functional swallowing ability and vice versa. Researching patients who start with severe dysphagia separately from those who do not, may provide more insight into the effectiveness of early dysphagia intervention for each respective group.

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As already mentioned, asking patients to rate swallowing pain rather than pain while doing the swallowing exercises limited our ability to interpret comfort level of each PSE program. It likely would have been more telling to ask patients about comfort, specifically while doing the swallowing exercises.

Furthermore, it may have been better to use the EAT-10 rather than the EAT-20 given that the EAT-10 had better reliability ratings than the EAT-20, and given that the EAT-20 did not have normative internal consistency data for the emotional, physical, and functional subscales. Analysis of the subscales using Chronbach's alpha and the data gathered in this investigation provided acceptable correlation levels within each subscale; however, due to the small sample size in this investigation, the results of the Chronbach's α should be interpreted with caution. Using the EAT-10 would have also reduced the time needed when gathering data from patients. This was particularly relevant when obtaining data in the middle and final stages of RT/CRT when patients were very sick. Patients' poor emotional and physical condition may have impacted their answers when giving data. Specifically, they may have rushed to complete the process more quickly. Using a shorter outcome measure such as the EAT-10 may have minimized this potential confound.

The inclusion of the Shaker exercise in both PSE programs could also be considered a weakness and warrants discussion. The Shaker exercise was included in both groups at the principal investigator's (PI) discretion due to the validity of the Shaker exercise for improving hyolaryngeal elevation and excursion and improving upper esophageal sphincter opening (Easterling et al., 2005; Logemann et al., 2009; Mepani et al., 2008; Shaker et al., 2002), both of which are common impairments in HNC patients (Hutcheson et al., 2008; Kotz et al., 2004; Logemann et al., 2008). This evidence, as well as the PI's clinical anecdotal evidence, compelled her to include the Shaker in both programs so that each patient could benefit from it. The concern of including the Shaker exercise in

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both programs was that it could have resulted in equivalent outcomes in both groups, had the Shaker been the primary contributor to the outcomes. However, this was not case, and therefore, inclusion of the Shaker in both programs should not take away from any of the conclusions. Certainly, it is possible that both groups benefitted from the Shaker and, therefore, between-group differences were smaller than they would have been had the Shaker not been included in the C-PSE group.

Adding a no-treatment control group certainly would have added confidence to the conclusions made based on the study results; however, ethically this was not possible given that sufficient evidence warrants use of a PSE program for all HNC patients undergoing RT/CRT (Carnaby-Mann et al., 2011; Carroll et al., 2008; Kotz et al., 2012; van der Molen et al., 2011; Virani et al., 2015). As discussed above, in comparison to the no-treatment control groups in prior PSE studies, and in comparison to non-PSE studies, the outcomes from both groups in the current study were better than outcomes of patients not completing PSEs.

Lastly, the investigators found it challenging to reliably measure compliance with the exercise programs. Patients frequently forgot to bring their exercise-tracking sheet to the data collection session or the sheet was not filled in correctly or completely. This was particularly the case during the initial months of the study. In the later stages of the study, the investigator emphasized the importance of obtaining accurate compliance data, which improved the reliability of patients providing such data. It is also impossible to know if the compliance data provided by patients was accurate. Patients may have had a tendency to inflate their compliance to avoid disappointing the researcher.

Chapter 6: Conclusions

Clinical Implications

This study provides additional insight in developing an optimal prophylactic dysphagia treatment for patients with HNC undergoing RT with or without adjunctive chemotherapy. This study compared a unique PSE program, an indirect (non-swallowing) exercise program (ID-PSE), to a more common PSE program that consists of both direct and indirect swallowing exercises (C-PSE). The results indicated that patients who completed ID-PSE had better self-perceived swallowing function and swallowing-related QOL as measured by the EAT-20 and the MDADI at one month post-RT/CRT than patients prescribed C-PSE. Interestingly, although this outcome supported the hypotheses in the study regarding swallowing function, the researchers hypothesized that improved swallowing function outcomes in the ID-PSE group would be due to improve compliance with an ID-PSE program, which was not found. It is not clear why the ID-PSE group performed better than the C-PSE group. The two PSE programs were relatively balanced in physiological targets and dosage, other than the ID-PSE program including an exercise for jaw range of motion and the C-PSE program not including such an exercise. However, it is difficult to imagine how this difference could explain the difference in swallowing function outcomes, particularly because none of the patients in the C-PSE group complained of significantly reduced jaw function, nor was reduced jaw function observed visually. Certainly it is possible that patients in the C-PSE group had reduced jaw mobility relative to patients in the ID-PSE group but a slight reduction in jaw mobility would not explain significant changes in overall swallowing function.

One likely explanation for the difference between the groups is the relative simplicity of the ID-PSE program over the C-PSE program, which likely contributed to patients completing the ID-PSE program more accurately than the C-PSE program. The effortful swallow in the C-PSE program can be

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particularly challenging for patients to do accurately and accuracy of the effortful swallow is difficult to assess without surface electromyography (Huckabee & Steele, 2006). Additionally, clinical experience indicates that the effortful swallow and the Mendelsohn maneuver are the most vulnerable swallowing exercises to be done incorrectly when a patient is fatigued and weak. Whereas, it is difficult to imagine how any of the ID-PSE exercises would have been significantly impacted by fatigue or weakness. Therefore, accurateness of the exercises, rather than the specific exercises themselves, may have contributed to the outcomes. A study contrasting a home PSE program with minimal monitoring of accuracy of each exercise (as in the current study) versus the same program with regular assessment of exercise accuracy would help answer this question.

This study provides preliminary evidence that a PSE program consisting solely of indirect exercises may be as effective as a PSE program consisting of a combination of direct and indirect swallowing exercises. This is a particularly interesting finding in light of principles of neuroplasticity, which indicate that direct (i.e., specific) exercises are more beneficial than indirect (i.e., non-specific) exercises (Kleim & Jones, 2008; Robbins et al., 2008). This study, and the many unanswered questions that follow it, by no means negate these current established principles of neuroplasticity; however, it does highlight the need for continued research in the area.

An additional clinical implication of the study applies to patients with severe dysphagia. Many patients with severe dysphagia are unable to reliably perform direct swallowing exercises due to inability to reliably elicit a swallow. This study provides additional evidence for the benefit of indirect swallowing exercises for these patients in particular.

Future Directions

This line of research is truly in its infancy. The current evidence base has primarily demonstrated proof-of-concept, safety, and feasibility. Hula, Cherney, and Worrall (2013) lay out a useful sequence for continued treatment efficacy research. Additional Phase 1 studies are needed to determine specification of a PSE protocol as well as optimal outcome measures. Research in this vein will answer questions regarding the most optimal swallowing exercises, the optimal dose and dose frequency of those exercises, the ideal timing of onset of a PSE program, and the most optimal outcome measures to be used in subsequent Phase II trials. Phase II trials can then commence to establish treatment efficacy. Phase II trials should include randomized control trials with an emphasis on making inferences at the population level using highly controlled research environments. There are many population factors that will need to be considered and controlled for in Phase II trials including tumor size and location, cancer stage, the presence of pre-RT/CRT surgery, age, gender, etc. The final two phases recommended by Hula et al. (2013) include Phase III trials, which are designed to determine treatment effectiveness under typical clinical practice conditions, and Phase IV trials, which have a goal of determining the need for change to standard health service delivery models or policy. Phase IV trials focus on answering questions surrounding cost-effectiveness and cost-benefit ratios.

There are also a whole host of psychosocial factors that play a role in treating patients with HNC. These factors will likely play a role in future research. As an example, anecdotally we observed that patients with a strong support network were more compliant with exercises and dealt with the negative impacts of RT/CRT better than patients who did not have a strong support network. Given this observation, we recommend that future research consider these factors, how they impact swallowing function outcomes, and how to identify at-risk patients due to poor social support.

References

- Ackerstaff, A. H., Balm, A. J. M., Rasch, C. R. N., de Boer, J. P., Wiggendaad, R., Rietveld, D. H. F., . . . Hilgers, F. J. M. (2009). First-year quality of life assessment of an intra-arterial (RADPLAT) versus intravenous chemoradiation phase III trial. *Head & Neck*, *31*(1), 77-84.
doi:10.1002/hed.20937
- Agarwal, J., Palwe, V., Dutta, D., Gupta, T., Laskar, S. G., Budrukhar, A., . . . Shrivastava, S. K. (2011). Objective assessment of swallowing function after definitive concurrent (chemo)radiotherapy in patients with head and neck cancer. *Dysphagia*, *26*, 399-406.
doi:10.1007/s00455-011-9326-4
- Agarwala, S., & Sbeitan, I. (2006). Iatrogenic swallowing disorders: Chemotherapy. In R. Carraue, & T. Murry (Eds.), *Comprehensive management of swallowing disorders* (pp. 129). San Diego, CA: Plural Publishing.
- Ahlberg, A., Engström, T., Nikolaidis, P., Gunnarsson, K., Johansson, H., Sharp, L., & Laurell, G. (2011). Early self-care rehabilitation of head and neck cancer patients. *Acta Oto-Laryngologica*, *131*(5), 552-561.
- Arraras, J. I., Arias, F., Tejedor, M., Pruja, E., Marcos, M., Martínez, E., & Valerdi, J. (2002). The EORTC QLQ-C30 (version 3.0) quality of life questionnaire: Validation study for Spain with head and neck cancer patients. *Psycho-Oncology*, *11*(3), 249-256.

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

- Auluck, A., Hislop, G., Bajdik, C., Poh, C., Zhang, L., & Rosin, M. (2010). Trends in oropharyngeal and oral cavity cancer incidence of human papillomavirus (HPV)-related and HPV-unrelated sites in a multicultural population. *Cancer, 116*(11), 2635-2644.
doi:10.1002/cncr.25087
- Baskar, R., Lee, K., Yeo, R., & Yeoh, K. (2012). Cancer and radiation therapy: Current advances and future directions. *International Journal of Medical Sciences, 9*(3), 193-199.
doi:10.7150/ijms.3635
- Belafsky, P. C., Mouadeb, D. A., Rees, C. J., Pryor, J. C., Postma, G. N., Allen, J., & Leonard, R. J. (2008). Validity and reliability of the eating assessment tool (EAT-10). *The Annals of Otolaryngology, Rhinology, and Laryngology, 117*(12), 919-924.
- Bjordal, K., de Graeff, A., Fayers, P. M., Hammerlid, E., van Pottelsberghe, C., Curran, D., . . . Kaasa, S. (2000). A 12 country field study of the EORTC QLQ-C30 (version 3.0) and. *European Journal of Cancer, 36*, 1796-1807.
- Bjordal, K., Hammerlid, E., Ahlner-Emqvist, M., de Graeff, A., Boysen, M., Evenson, J., . . . Kaasa, S. (1999). Quality of life in head and neck cancer patients: Validation of the European organization for research and treatment of cancer quality of life questionnaire-H&N35. *Journal of Clinical Oncology, 17*(3), 1008-1019.
- Bjordal, K., & Kaasa. (1992). Psychometric validation of the EORTC core quality of life questionnaire, 30-item version and A diagnosis-specific module for head and neck cancer

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

patients. *Acta Oncologica*, 31(3), 311-320. Retrieved from

<http://informahealthcare.com/doi/abs/10.3109/02841869209108178>

Bleier, B. S., Levine, M. S., Mick, R., Rubesin, S. E., Sack, S. Z., McKinney, K., & Mirza, N. (2007). Dysphagia after chemoradiation: Analysis by modified barium swallow. *The Annals of Otolaryngology, Rhinology, and Laryngology*, 116(11), 837-841.

Borget, I., Abramowitz, L., & Mathevet, P. (2011). Economic burden of HPV-related cancers in France. *Vaccine*, 29(32), 5245-5249. doi:10.1016/j.vaccine.2011.05.018

Braam, P. M., Roesink, J. M., Moerland, M. A., Raaijmakers, C. P. J., Schipper, M., & Terhaard, C. H. J. (2005). Long-term parotid gland function after radiotherapy. *International Journal of Radiation Oncology*Biology*Physics*, 62(3), 659-664. doi:10.1016/j.ijrobp.2004.12.015

Buchbinder, D., Currivan, R. B., Kaplan, A. J., & Urken, M. L. (1993). Mobilization regimens for the prevention of jaw hypomobility in the irradiated patient: A comparison of three techniques. *Journal of Oral and Maxillofacial Surgery*, 51(8), 863-867. doi:10.1016/S0278-2391(10)80104-1

Büntzel, J., Glatzel, M., Mücke, R., Micke, O., & Bruns, F. (2007). Influence of amifostine on late radiation-toxicity in head and neck cancer - A follow-up study. *Anticancer Research*, 27(4A), 1953-1956.

Carnaby-Mann, G., & Crary, M. (2010). McNeill dysphagia therapy program: A case-control study. *Archives of Physical Medicine and Rehabilitation*, 91(5), 743-749.

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

- Carnaby-Mann, G., Crary, M., Schmalfluss, I., & Amdur, R. (2011). "Pharyngocise": Randomized controlled trial of preventative exercises to maintain muscle structure and swallowing function during head-and-neck chemoradiotherapy. *Head and Neck*, 83, 210-219.
doi:10.1016/j.ijrobp.2011.06.1954
- Carroll, W. R., Locher, J. L., Canon, C. L., Bohannon, I. A., McColloch, N. L., & Magnuson, J. S. (2008). Pretreatment swallowing exercises improve swallow function after chemoradiation. *The Laryngoscope*, 118(1), 39-43.
- Chang, Y., Chen, S., Lui, L. T., Wang, T., Wang, T., Hsiao, T., . . . Lien, I. (2003). Dysphagia in patients with nasopharyngeal cancer after radiation therapy: A videofluoroscopic swallowing study. *Dysphagia*, 18(2), 135-143.
- Chaturvedi, A., Engels, E. A., Anderson, W. F., & Gillison, M. L. (2008). Incidence trends for human papillomavirus-related and -unrelated oral squamous cell carcinomas in the united states. *Journal of Clinical Oncology*, 26(4), 612-619.
- Chaturvedi, A., Engels, E., Pfeiffer, R., Hernandez, B., Xiao, W., Kim, E., . . . Gillison, M. (2011). Human papillomavirus and rising oropharyngeal cancer incidence in the united states. *Journal of Clinical Oncology*, 32(10), 4294-4301. Retrieved from <http://pop.oralcancerfoundation.org/hpv/pdf/hpv-and-rising-incidence-in-us-2011.pdf>
- Chen, A. Y., Frankowski, R., Bishop-Leone, J., Hebert, T., Leyk, S., Lewin, J., & Goepfert. (2001). The development and validation of a dysphagia-specific quality of life questionnaire

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

for patients with head and neck cancer. *Archives of Otolaryngology--Head & Neck Surgery*, 127(7), 870-876.

Cheng, S. S., Terrell, J. E., Bradford, C. R., Ronis, D. L., Fowler, K. E., Prince, M. E., . . . Duffy, S. A. (2006). Variables associated with feeding tube placement in head and neck cancer. *Archives of Otolaryngology - Head & Neck Surgery*, 132(6), 655-661.

Chesson, H. W., Ekwueme, D. U., Saraiya, M., Watson, M., Lowy, D. R., & Markowitz, L. E. (2012). Estimates of the annual direct medical costs of the prevention and treatment of disease associated with human papillomavirus in the united states. *Vaccine*, 30(42), 6016-6019. doi:10.1016/j.vaccine.2012.07.056

Chie, W. C., Hong, R. L., Lai, C. C., Ting, L. L., & Hsu, M. M. (2003). Quality of life in patients of nasopharyngeal carcinoma: Validation of the Taiwan Chinese version of the EORTC QLQ-C30 and the EORTC QLQ-H&N35. *Quality of Life Research*, 12(1), 93-98. Retrieved from <http://www.jstor.org/page/info/about/policies/terms.jsp>

Clark, H. M., O'Brien, K., Calleja, A., & Corrie, S. N. (2009). Effects of directional exercise on lingual strength. *Journal of Speech, Language, and Hearing Research : JSLHR*, 52(4), 1034-47.

Cohen, E. G., Deschler, D. G., Walsh, K., & Hayden, R. E. (2005). Early use of a mechanical stretching device to improve mandibular mobility after composite resection: A pilot study. *Archives of Physical Medicine and Rehabilitation*, 86(7), 1416-1419. doi:10.1016/j.apmr.2004.10.035

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

Cohen-Mansfield, J., Marx, M., & Guralnik, J. (2003). Motivators and barriers to exercise in an older community-dwelling population. *Journal of Aging and Physical Activity*, 11, 242-253.

Retrieved from

<http://www.humankinetics.com/AcuCustom/Sitename/Documents/DocumentItem/1242.pdf>

Colodny, N. (2002). Interjudge and intrajudge reliabilities in fiberoptic endoscopic evaluation of swallowing (FEES) using the penetration-aspiration scale: A replication study. *Dysphagia*, 17(4), 308-315.

Crary, M., Carnaby, G., LaGorio, L., & Carvajal, P. (2012). Functional and physiological outcomes from an exercise-based dysphagia therapy: A pilot investigation of the McNeill dysphagia therapy program. *Dysphagia Therapy*, 93(7), 1173-1178.

doi:10.1016/j.apmr.2011.11.008

Crary, M., Mann, G. D. C., & Groher, M. E. (2005). Initial psychometric assessment of a functional oral intake scale for dysphagia in stroke patients. *Archives of Physical Medicine and Rehabilitation*, 86(8), 1516-1520.

D'Antonio, L. L., Zimmerman, G. J., Cella, D. F., & Long, S. A. (1996). Quality of life and functional status measures in patients with head and neck cancer. *Archives of Otolaryngology-Head & Neck Surgery*, 122(5), 482-487.

doi:10.1001/archotol.1996.01890170018005

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

- de Castro Jr., G., & Honda Federico, M. (2006). Evaluation, prevention and management of radiotherapy-induced xerostomia in head and neck cancer patients. *Oncology*, 18(3), 266-270.
- de Graeff, A., de Leeuw, R. J., Ros, W. J. G., Hordijk, G., Battermann, J. J., Blijham, G. H., & Winnubst, J. A. M. (1999). A prospective study on quality of life of laryngeal cancer patients treated with radiotherapy. *Head and Neck*, 21(4), 291-296.
- Delanian, S., & Lefaix, J. (2004). The radiation-induced fibroatrophic process: Therapeutic perspective via the antioxidant pathway. *Radiotherapy and Oncology*, 73(2), 119-131.
doi:10.1016/j.radonc.2004.08.021
- Delanian, S., & Lefaix, J. (2007). Current management for late normal tissue injury: Radiation-induced fibrosis and necrosis. *Seminars in Radiation Oncology*, 17(2), 99-107.
- Department of Veteran Affairs Laryngeal Cancer Study Group. (1991). Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. *New England Journal of Medicine*, 324(24), 1685-1690.
doi:10.1056/NEJM199106133242402
- Dijkstra, P. U., Sterken, M. W., Pater, R., Spijkervet, F. K. L., & Roodenburg, J. L. N. (2007). Exercise therapy for trismus in head and neck cancer. *Oral Oncology*, 43(4), 389-394.
doi:10.1016/j.oraloncology.2006.04.003
- Easterling, C., Grande, B., Kern, M., Sears, K., & Shaker, R. (2005). Attaining and maintaining isometric and isokinetic goals of the shaker exercise. *Dysphagia*, 20(2), 133-138.

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

Eisbruch, A. (2005). Intensity-modulated radiation therapy in the treatment of head and neck cancer. *Nature Reviews Clinical Oncology*, 2(1), 34-39. doi:10.1038/nrponc0058

Eisbruch, A., Lyden, T., Bradford, C. R., Dawson, L. A., Haxer, M. J., Miller, A. E., . . . Wolf, G. T. (2002). Objective assessment of swallowing dysfunction and aspiration after radiation concurrent with chemotherapy for head-and-neck cancer. *International Journal of Radiation Oncology*Biophysics*Physics*, 53(1), 23-28. doi:10.1016/S0360-3016(02)02712-8

El-Deiry, M. W., Futran, N. D., McDowell, J. A., Weymuller Jr, E. A., & Yueh, B. (2009). Influences and predictors of long-term quality of life in head and neck cancer survivors. *Head and Neck*, 135(4), 380-384.

Elting, L. S., Keefe, D. M., Sonis, S. T., Garden, A. S., Spijkervet, F. K. L., Barasch, A., . . . Vera-Llonch, M. (2008). Patient-reported measurements of oral mucositis in head and neck cancer patients treated with radiotherapy with or without chemotherapy. *Head and Neck*, 113(10), 2704-2713. doi:10.1002/cncr.23898

Field, A. (2013a). The beast of bias. *Discovering statistics using IBM SPSS statistics* (4th Ed ed., pp. 172). Los Angeles, CA: Sage.

Field, A. (2013b). Categorical data. *Discovering statistics using IBM SPSS statistics* (pp. 723-724). Los Angeles, CA: Sage.

Field, A. (2013c). Non-parametric models. *Discovering statistics using IBM SPSS statistics* (pp. 227). Los Angeles, CA: Sage.

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

Forastiere, A., Koch, W., Trotti, A., & Sidransky, D. (2001). Head and neck cancer. *The New England Journal of Medicine*, 345(26), 1890-1900.

Forastiere, A., Goepfert, H., Maor, M., Pajak, T., Weber, R., Morrison, W., & Glisson, B. (2003a). Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. *The New England Journal of Medicine*, 349(22), 2091-2098.

Forastiere, A., Goepfert, H., Maor, M., Pajak, T., Weber, R., Morrison, W., & Glisson, B. (2003b). Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. *New England Journal of Medicine*, 349(22), 2091-2098.

Francis, D., Weymuller, E., Parvathaneni, U., Merati, A., & Yueh, B. (2010). Dysphagia, stricture, and pneumonia in head and neck cancer patients: Does treatment modality matter? *The Annals of Otolaryngology, Rhinology, and Laryngology*, 119(6), 391-397. Retrieved from <http://europepmc.org/abstract/med/20583737>

Franzmann, E. J., Lundy, D. S., Abitbol, A. A., & Goodwin, W. J. (2006). Complete hypopharyngeal obstruction by mucosal adhesions: A complication of intensive chemoradiation for advanced head and neck cancer. *Head & Neck*, 28(8), 663-670.

Frowen, J. J., & Perry, A. R. (2006). Swallowing outcomes after radiotherapy for head and neck cancer: A systematic review. *Head & Neck*, 28(10), 932-44.

Fujiu, M., & Logemann, J. (1996). Effect of a tongue-holding maneuver on posterior pharyngeal wall movement during deglutition. *American Journal of Speech-Language Pathology / American Speech-Language-Hearing Association*, 5(1), 23-30.

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

Fuller, S. C., Leonard, R., Aminpour, S., & Belafsky, P. C. (2009). Validation of the pharyngeal squeeze maneuver. *Otolaryngology - Head and Neck Surgery*, 140(3), 391-394.

Garcie-Peris, P., L. Paron, C. Velasco, C. de la Cuerda, M. Camblor, I. Breton, . . . P. Clave. (2007). Long-term prevalence of oropharyngeal dysphagia in head and neck cancer patients: Impact on quality of life. *Clinical Nutrition*, 26, 710-717. doi:10.1016/j.clnu.2007.08.006

Gaziano, J. E. (2002). Evaluation and management of oropharyngeal dysphagia in head and neck cancer. *Cancer Control*, 9(5), 400-409.

Gillespie, M. B., Brodsky, M. B., Day, T. A., Lee, F., & Martin-Harris, B. (2004). Swallowing-related quality of life after head and neck cancer treatment. *The Laryngoscope*, 114(8), 1362-1367. doi:10.1097/00005537-200408000-00008

Goguen, L. A., Posner, M. R., Norris, C. M., Tishler, R. B., Wirth, L. J., Annino, D. J., . . . Haddad, R. I. (2006). Dysphagia after sequential chemoradiation therapy for advanced head and neck cancer. *Otolaryngology--Head and Neck Surgery*, 134(6), 916-922.

Greven, K. M., White, D. R., Browne, J. D., Williams, D. W., McGuirt, W. F., & D'Agostino, R. B. (2008). Swallowing dysfunction is a common sequelae after chemoradiation for oropharynx carcinoma. *American Journal of Clinical Oncology*, 31(3), 209-212.

Groher, M., & Crary, M. (2010). *Dysphagia: Clinical management in adults and children*. Maryland Heights, Missouri: Mosby, Inc.

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

- Gurney, T. A., Eisele, D. W., Orloff, L. A., & Wang, S. J. (2008). Predictors of quality of life after treatment for oral cavity and oropharyngeal carcinoma. *Otolaryngology - Head and Neck Surgery*, 139(2), 262-267.
- Hammerlid, E., Silander, E., Hörnemark, L., & Sullivan, M. (2001). Health-related quality of life three years after diagnosis of head and neck cancer - a longitudinal study. *Head & Neck*, 23(2), 113-125.
- Harrison, L. B., Zelefsky, M. J., Pfister, D. G., Carper, E., Raben, A., Kraus, D. H., . . . Portenoy, R. (1997). Detailed quality of life assessment in patients treated with primary radiotherapy for squamous cell cancer of the base of the tongue. *Head & Neck*, 19(3), 169-175.
- Hind, J. A., Nicosia, M. A., Roecker, E. B., Carnes, M. L., & Robbins, J. (2001). Comparison of effortful and noneffortful swallows in healthy middle-aged and older adults. *Archives of Physical Medicine and Rehabilitation*, 82(12), 1661-1665.
- Hiss, S. G., & Huckabee, M. L. (2005). Timing of pharyngeal and upper esophageal sphincter pressures as a function of normal and effortful swallowing in young healthy adults. *Dysphagia*, 20(2), 149-156. doi:10.1007/s00455-005-0008-y
- Huckabee, M., Butler, S. G., Barclay, M., & Jit, S. (2005). Submental surface electromyographic measurement and pharyngeal pressures during normal and effortful swallowing. *Archives of Physical Medicine and Rehabilitation*, 86(11), 2144-9.

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

- Huckabee, M., & Steele, C. M. (2006). An analysis of lingual contribution to submental surface electromyographic measures and pharyngeal pressure during effortful swallow. *Archives of Physical Medicine and Rehabilitation*, 87(8), 1067-72.
- Hula, W. D., Cherney, L. R., & Worrall, L. E. (2013). Setting a research agenda to inform intensive comprehensive aphasia programs. *Topics in Stroke Rehabilitation*, 20(5), 409-420. doi:10.1310/tsr2005-409
- Hutcheson, K. A., & Lewin, J. S. (2012). Functional outcomes after chemoradiotherapy of laryngeal and pharyngeal cancers. *Current Oncology Reports*, 14(2), 158-165.
- Hutcheson, K. A., Barringer, D. A., Rosenthal, D. I., May, A. H., Roberts, D. B., & Lewin, J. S. (2008). Swallowing outcomes after radiotherapy for laryngeal carcinoma. *Archives of Otolaryngology--Head & Neck Surgery*, 134(2), 178-183.
- Ishiki, H., Onozawa, Y., Kojima, T., Hironaka, S., Fukutomi, A., Yasui, H., . . . Nishimura, T. (2012). Nutrition support for head and neck squamous cell carcinoma patients treated with chemoradiotherapy: How often and how long? *International Scholarly Research Network Oncology*, 2012, 1-5. doi:10.5402/2012/274739
- Jensen, K., Lambertsen, K., & Grau, C. (2007). Late swallowing dysfunction and dysphagia after radiotherapy for pharynx cancer: Frequency, intensity and correlation with dose and volume parameters. *Radiotherapy and Oncology*, 85(1), 74-82. doi:10.1016/j.radonc.2007.06.004
- Jensen, S. B., Pedersen, A. M. L., Vissink, A., Andersen, E., Brown, C. G., Davies, A. N., . . . Brennan, M. T. (2010). A systematic review of salivary gland hypofunction and xerostomia

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

induced by cancer therapies: Prevalence, severity and impact on quality of life. *Support Care Cancer*, 18(8), 1039-1060. doi:10.1007/s00520-010-0827-8

Johnson, D., Herring, H., & Daniels, S. (2014). Dysphagia management in stroke rehabilitation. *Current Physical Medicine and Rehabilitation Reports*, 2(4), 207-218. doi:10.1007/s40141-014-0059-9

Kahrilas, P. J., Logemann, J., Krugler, C., & Flanagan, E. (1991). Volitional augmentation of upper esophageal sphincter opening during swallowing. *American Journal of Physiology*, 260(3), 450-456.

Kent, M. L., Brennan, M. T., Noll, J. L., Fox, P. C., Burri, S. H., Hunter, J. C., & Lockhart, P. B. (2007). Radiation-induced trismus in head and neck cancer patients. *Supportive Care in Cancer*, 16(3), 305-309. doi:10.1007/s00520-007-0345-5

Kent, R., Kent, J., & Rosenbek, J. (1987). Maximum performance tests of speech production. *Journal of Speech and Hearing Disorders*, 52, 367-387. doi:10.1044/jshd.5204.367

Kleim, J. A., & Jones, T. A. (2008). Principles of experience-dependent neural plasticity: Implications for rehabilitation after brain damage. *Journal of Speech, Language, and Hearing Research*, 51(1), 225-239.

Koh, G. C., Saxena, S. K., Ng, T., Yong, D., & Fong, N. (2012). Effect of duration, participation rate, and supervision during community rehabilitation on functional outcomes in the first poststroke year in singapore. *Archives of Physical Medicine and Rehabilitation*, 93(2), 279-286. doi:10.1016/j.apmr.2011.08.017

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

- Koiwai, K., Shikama, N., Sasaki, S., Shinoda, A., & Kadoya, M. (2010). Validation of the total dysphagia risk score (TDRS) as a predictive measure for acute swallowing dysfunction induced by chemoradiotherapy for head and neck cancers. *Radiotherapy and Oncology*, 97(1), 132-135. doi:10.1016/j.radonc.2010.08.006
- Kotz, T., Abraham, S., Beitler, J. J., Wadler, R. S., & Smith, R. V. (1999). Pharyngeal transport dysfunction consequent to an organ-sparing protocol. *Archives of Otolaryngology–Head & Neck Surgery*, 125(4), 410-413. doi:10.1001/archotol.125.4.410
- Kotz, T., Costello, R., Li, Y., & Posner, M. R. (2004). Swallowing dysfunction after chemoradiation for advanced squamous cell carcinoma of the head and neck. *Head & Neck*, 26(4), 365-372.
- Kotz, T., Federman, A. D., Kao, J., Milman, L., Packer, S., Lopez-Prieto, C., . . . Genden, E. M. (2012). Prophylactic swallowing exercises in patients with head and neck cancer undergoing chemoradiation: A randomized trial. *Archives of Otolaryngology - Head & Neck Surgery*, 138(4), 376-342.
- Kulbersh, B. D. (2006). Pretreatment, preoperative swallowing exercises may improve dysphagia quality of life. *The Laryngoscope*, 116(6), 883-886.
- Langmore, S. E., & Krisciunas, G. P. (2010). Dysphagia after radiotherapy for head and neck cancer: Etiology, clinical presentation, and efficacy of current treatments. *Perspectives on Swallowing and Swallowing Disorders*, 19(2), 32-38.

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

Lazarus, C. (2000). Management of swallowing disorders in head and neck cancer patients:

Optimal patterns of care. *Seminars in Speech and Language*, 21(4), 293-309.

Lazarus, C., Husaini, H., Falciglia, D., DeLacure, M., Branski, R. C., Kraus, D., . . . Sanfilippo,

N. (2014). Effects of exercise on swallowing and tongue strength in patients with oral and oropharyngeal cancer treated with primary radiotherapy with or without chemotherapy.

International Journal of Oral and Maxillofacial Surgery, 43(5), 523-530.

doi:10.1016/j.ijom.2013.10.023

Lazarus, C., Logemann, J., & Gibbons, P. (1993). Effects of maneuvers on swallow functioning in

a dysphagic oral cancer patient. *Head and Neck*, 15(5), 419-424.

Lazarus, C., Logemann, J., Pauloski, B., Rademaker, A. W., Helenowski, I. B., Vonesh, E. F., . . .

Haraf, D. J. (2007). Effects of radiotherapy with or without chemotherapy on tongue strength and swallowing in patients with oral cancer. *Head & Neck*, 29(7), 632-637.

doi:10.1002/hed.20577

Lazarus, C., Logemann, J., Pauloski, B., Rademaker, A. W., Larson, C. R., Mittal, B. B., &

Pierce, M. (2000). Swallowing and tongue function following treatment for oral and oropharyngeal cancer. *Journal of Speech, Language, and Hearing Research*, 43, 1011-1023.

doi:1092-4388/00/4304-1011

Lazarus, C., Logemann, J., Wook Song, C., Rademaker, A. W., & Kahrilas, P. J. (2002). Effects

of voluntary maneuvers on tongue base function for swallowing. *Folia Phoniatrica Et*

Logopaedica, 54(4), 171-176.

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

Leder, S. B., Sasaki, C. T., & Burrell, M. I. (1998). Fiberoptic endoscopic evaluation of dysphagia to identify silent aspiration. *Dysphagia*, 13(1), 19-21.

Lee, J., Machtay, M., Unger, L. D., Weinstein, G. S., Weber, R. S., Chalian, A. A., & Rosenthal, D. I. (1998). Prophylactic gastrostomy tubes in patients undergoing intensive irradiation for cancer of the head and neck. *Archives of Otolaryngology - Head & Neck Surgery*, 124(8), 871-875.

Lee, N., & Terezakis, S. (2008). Intensity-modulated radiation therapy. *Journal of Surgical Oncology*, 97(8), 691-696. doi:10.1002/jso.21014

Lever, T. E., Cox, K. T., Holbert, D., Shahrier, M., Hough, M., & Kelley-Salamon, K. (2007). The effect of an effortful swallow on the normal adult esophagus. *Dysphagia*, 22(4), 312-325. doi:10.1007/s00455-007-9107-2

List, M. A., D'Antonio, L. L., Cella, D. F., Siston, A., Mumby, P., Haraf, D., & Vokes, E. (1996). The performance status scale for head and neck cancer patients and the functional assessment of cancer therapy-head and neck scale. *American Cancer Society*, 77(11), 2294-2301.

List, M. A., Mumby, P., Haraf, D., Siston, A., Mick, R., MacCracken, E., & Vokes, E. (1997). Performance and quality of life outcome in patients completing concomitant chemoradiotherapy protocols for head and neck cancer. *Quality of Life Research*, 6(3), 274-284.

List, M. A., Siston, A., Haraf, D., Schumm, P., Kies, M., Stenson, K., & Vokes, E. E. (1999). Quality of life and performance in advanced head and neck cancer patients on concomitant

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

chemoradiotherapy: A prospective examination. *Journal of Clinical Oncology*, 17(3), 1020-1028.

List, M. A., Ritter-Sterr, C., & Lansky, S. B. (1990). A performance status scale for head and neck cancer patients. *Cancer*, 66(3), 564-569. doi:AID-CNCR2820660326>3.0.CO;2-D

Loeb, M. B., Becker, M., Eady, A., & Walker-Dilks, C. (2003). Interventions to prevent aspiration pneumonia in older adults: A systematic review. *Journal of the American Geriatrics Society*, 51(7), 1018-1022. doi:10.1046/j.1365-2389.2003.51318.x

Logemann, J. (1997). Role of the modified barium swallow in management of patients with dysphagia. *Otolaryngology - Head and Neck Surgery*, 116(3), 335-338. doi:10.1016/S0194-5998(97)70269-9

Logemann, J. (1998). *Evaluation and treatment of swallowing disorders* (2nd ed.). Austin, TX: Pro-Ed.

Logemann, J., Pauloski, B., Rademaker, A. W., & Colangelo, L. A. (1997). Speech and swallowing rehabilitation for head and neck cancer patients. *Oncology (Williston Park, N.Y.)*, 11(5), 651-659.

Logemann, J., Pauloski, B., Rademaker, A. W., Lazarus, C., Gaziano, J., Stachowiak, L., . . .

Mittal, B. (2008). Swallowing disorders in the first year after radiation and chemoradiation. *Head & Neck*, 30(2), 148-158. doi:10.1002/hed.20672

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

Logemann, J., Rademaker, A., Pauloski, B., Kelly, A., Stangl-McBreen, C., Antinoja, J., . . .

Shaker, R. (2009). A randomized study comparing the shaker exercise with traditional therapy: A preliminary study. *Dysphagia*, 24(4), 403-411.

Mallick, I., & Waldron, J. N. (2009). Radiation therapy for head and neck cancers. *Seminars in Oncology Nursing*, 25(3), 193-202. doi:10.1016/j.soncn.2009.05.002

Mann whitney U test in SPSS. Retrieved from <https://statistics.laerd.com/premium/mwut/mann-whitney-test-in-spss-12.php>

Marur, S., D'Souza, G., Westra, W. H., & Forastiere, A. A. (2010). HPV-associated head and neck cancer: A virus-related cancer epidemic. *Lancet Oncology*, 11(8), 781-789.

Maurer, J., Hipp, M., Schafer, C., & Kolbl, O. (2011). Dysphagia - impact on quality of life after radio(chemo)therapy of head and neck cancer. *Strahlentherapie Und Onkologie*, 187(11), 744-749.

McColloch, N. L., Carroll, W. R., & Magnuson, J. S. (2010). Pretreatment dysphagia protocol for the patient with head and neck cancer undergoing chemoradiation. *Perspectives on Swallowing and Swallowing Disorders*, 19(2), 53-56.

Mepani, R., Antonik, S., Massey, B., Kern, M., Logemann, J., Pauloski, B., . . . Shaker, R. (2008). Augmentation of deglutitive thyrohyoid muscle shortening by the shaker exercise. *Dysphagia*, 24(1), 26-31. doi:10.1007/s00455-008-9167-y

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

- Milas, L., Mason, K. A., Liao, Z., & Ang, K. K. (2003). Chemoradiotherapy: Emerging treatment improvement strategies. *Head & Neck*, 25(2), 152-167. doi:10.1002/hed.10232
- Miloro, K. V., Langmore, S. E., & Pearson Jr, W. G. (2014). Effortful pitch glide: A potential new exercise evaluated by dynamic MRI. *Journal of Speech, Language, and Hearing Research*, 57, 1243-1250.
- Murphy, B. A., & Gilbert, J. (2009). Dysphagia in head and neck cancer patients treated with radiation: Assessment, sequelae, and rehabilitation. *Seminars in Radiation Oncology*, 19(1), 35-42.
- Murry, T., & Carrau, R. (2006). *Clinical management of swallowing disorders* (2nd ed.). San Diego, CA: Plural Publishing.
- Newman, L. A., Vieira, F., Schwiezer, V., Samant, S., Murry, T., Woodson, G., . . . Robbins, K. T. (1998). Eating and weight changes following chemoradiation therapy for advanced head and neck cancer. *Archives of Otolaryngology - Head & Neck Surgery*, 124(5), 589-592.
- Nguyen, N. P., Frank, C., Moltz, C. C., Vos, P., Smith, H. J., Nguyen, P. D., . . . Sallah, S. (2009). Analysis of factors influencing aspiration risk following chemoradiation for oropharyngeal cancer. *British Journal of Radiology*, 82, 675-680. doi:10.1259/bjr/72852974
- Nguyen, N. P., Frank, C., Moltz, C. C., Vos, P., Smith, H. J., Bhamidipati, P. V., . . . Sallah, S. (2006). Aspiration rate following chemoradiation for head and neck cancer: An underreported occurrence. *Radiotherapy and Oncology : Journal of the European Society for Therapeutic Radiology and Oncology*, 80(3), 302-306.

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

Oates, J. E., Clark, J. R., Read, J., Reeves, N., Gao, K., Jackson, M., . . . O'brien, C. J. (2007).

Prospective evaluation of quality of life and nutrition before and after treatment for nasopharyngeal carcinoma. *Archives of Otolaryngology - Head & Neck Surgery*, 133(6), 533-540.

Olney, S. J., Nymark, J., Brouwer, B., Culham, E., Day, A., Heard, J., . . . Parvataneni, K. (2006).

A randomized controlled trial of supervised versus unsupervised exercise programs for ambulatory stroke survivors. *Stroke*, 37(2), 476-481.

doi:10.1161/01.STR.0000199061.85897.b7

Osoba, D., Aaronson, N., Zee, B., Sprangers, M., & Velde, A. t. (1997). Modification of the

EORTC QLQ-C30 (version 2.0) based on content validity and reliability testing in large samples of patients with cancer. *Quality of Life Research*, 6(2), 103-108. doi:1026429831234

O'Sullivan, B., & Levin, W. (2003). Late radiation-related fibrosis: Pathogenesis, manifestations, and current management. *Seminars in Radiation Oncology*, 13(3), 274-289.

Paleri, V., & Patterson, J. (2010). Use of gastrostomy in head and neck cancer: A systematic review to identify areas for future research. *Clinical Otolaryngology*, 35(3), 177-189.

Paleri, V., Roe, J. W. G., Strojan, P., Corry, J., Grégoire, V., Hamoir, M., . . . Ferlito, A. (2014).

Strategies to reduce long-term postchemoradiation dysphagia in patients with head and neck cancer: An evidence-based review. *Head & Neck*, 36(3), 431-443. doi:10.1002/hed.23251

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

- Patterson, J., & Wilson, J. A. (2011). The clinical value of dysphagia preassessment in the management of head and neck cancer patients. *Current Opinion in Otolaryngology & Head and Neck Surgery*, 19(3), 177-81. doi:10.1097/MOO.0b013e328345aeb0
- Pauloski, B. (2008). Rehabilitation of dysphagia following head and neck cancer. *Physical Medicine and Rehabilitation Clinics of North America*, 19(4), 889-928. doi:10.1016/j.pmr.2008.05.010
- Pauloski, B., Rademaker, A. W., Logemann, J., Stein, D., Beery, Q., Newman, L., . . . MacCracken, E. (2000). Pretreatment swallowing function in patients with head and neck cancer. *Head & Neck*, 22(5), 474-482.
- Pauloski, B., Rademaker, A. W., Logemann, J., Newman, L., MacCracken, E., Gaziano, J., & Stachowiak, L. (2006). Relationship between swallow motility disorders on videofluorography and oral intake in patients treated for head and neck cancer with radiotherapy with or without chemotherapy. *Head & Neck*, 28(12), 1069-1076.
- Pero-Cebollero, M., & Guardia-Olmos, J. (2013). The adequacy of different robust statistical tests in comparing two independent groups. *Psicologica*, 34, 407-424.
- Peterson, R. A. (1994). A meta-analysis of cronbach's coefficient alpha. *Journal of Consumer Research*, 21(2), 381-391. Retrieved from <http://www.jstor.org/stable/2489828>
- Pollock, M., Gaesser, G., Butcher, J., Despres, J., Dishman, R., Franklin, B., & Garber, C. (1998). ACSM position stand: The recommended quantity and quality of exercise for developing and

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults.

Medicine & Science in Sports and Exercise, 30(6), 975-991.

Pouderoux, P., & Kahrilas, P. J. (1995). Deglutitive tongue force modulation by volition, volume, and viscosity in humans. *Gastroenterology*, 108(5), 1418-26.

Rieger, J. M., Zalmanowitz, J. G., & Wolfaardt, J. F. (2006). Functional outcomes after organ preservation treatment in head and neck cancer: A critical review of the literature.

International Journal of Oral and Maxillofacial Surgery, 35(7), 581-587.

Ringash, J., Lockwood, G., O'Sullivan, B., Warde, P., Bayley, A., Cummings, B., . . . Waldron, J. (2008). Hyperfractionated, accelerated radiotherapy for locally advanced head and neck cancer: Quality of life in a prospective phase I/II trial. *Radiotherapy and Oncology*, 87(2), 181-187.

Robbins, J., Butler, S. G., Daniels, S., Gross, R. D., Langmore, S., & Lazarus, C. (2008).

Swallowing and dysphagia rehabilitation: Translating principles of neural plasticity into clinically oriented evidence. *Journal of Speech, Language, and Hearing Research*, 51(1), 276-300.

Robbins, J., Gangnon, R. E., Theis, S. M., Kays, S. A., Hewitt, A. L., & Hind, J. A. (2005). The effects of lingual exercise on swallowing in older adults. *Journal of the American Geriatrics Society*, 53(9), 1483-9.

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

- Robbins, J., Kays, S. A., Gangnon, R. E., Hind, J. A., Hewitt, A. L., Gentry, L. R., & Taylor, A. J. (2007). The effects of lingual exercise in stroke patients with dysphagia. *Archives of Physical Medicine and Rehabilitation*, 88(2), 150-158. doi:10.1016/j.apmr.2006.11.002
- Rodriguez-Caballero, A., Torres-Lagares, M., Robles-Garcia, J., Pachon-Ibanez, J., Gonzalez-Padilla, J., & Gutierrez-Perez, L. (2011). Cancer treatment-induced oral: A critical review. *Oral Medicine*, 41, 225-238. doi:10.1016/j.ijom.2011.10.011
- Roe, J. W. G., & Ashforth, K. M. (2011). Prophylactic swallowing exercises for patients receiving radiotherapy for head and neck cancer. *Current Opinion in Otolaryngology & Head and Neck Surgery*, 19(3), 144-149.
- Roe, J. W. G., Carding, P. N., Rhys-Evans, P. H., Newbold, K. L., Harrington, K. J., & Nutting, C. M. (2012). Assessment and management of dysphagia in patients with head and neck cancer who receive radiotherapy in the united kingdom -- A web-based survey. *Oral Oncology*, 48, 343-348. doi:10.1016/j.oraloncology.2011.11.003
- Rogers, S. N., Ahad, S. A., & Murphy, A. P. (2007). A structured review and theme analysis of papers published on 'quality of life' in head and neck cancer: 2000-2005. *Oral Oncology*, 43(9), 843-868.
- Rosenbek, J. C., Robbins, J. A., Roecker, E. B., Coyle, J. L., & Wood, J. L. (1996). A penetration-aspiration scale. *Dysphagia*, 11(2), 93-98. doi:10.1007/BF00417897
- Samant, S., Kumar, P., Wan, J., Hanchett, C., Vieira, F., Murry, T., . . . Robbins, K. T. (1999). Concomitant radiation therapy and targeted cisplatin chemotherapy for the treatment of

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

advanced pyriform sinus carcinoma: Disease control and preservation of organ function.

Head & Neck, 21(7), 595-601.

Schatz, K., Langmore, S. E., & Olson, N. (1991). Endoscopic and videofluoroscopic evaluations of swallowing and aspiration. *Annals of Otolaryngology, Rhinology & Laryngology*, 100(8), 678-681. doi:10.1177/000348949110000815

Seiwert, T. Y., Salama, J. K., & Vokes, E. E. (2007a). The chemoradiation paradigm in head and neck cancer. *Nature Clinical Practice Oncology*, 4(3), 156-171. doi:10.1038/ncponc0750

Seiwert, T. Y., Salama, J. K., & Vokes, E. E. (2007b). The concurrent chemoradiation paradigm—general principles. *Nature Clinical Practice Oncology*, 4(2), 86-100. doi:10.1038/ncponc0714

Shaker, R., Kern, M., Bardan, E., Taylor, A., Stewart, E., Hoffman, R., . . . Bonnevier, J. (1997). Augmentation of deglutitive upper esophageal sphincter opening in elderly by exercise. *The American Journal of Physiology*, 272(6), G1518-G1522. Retrieved from <http://ajpgi.physiology.org/content/ajpgi/272/6/G1518.full.pdf>

Shaker, R., Easterling, C., Kern, M., Nitschke, T., Massey, B., Daniels, S., . . . Dikeman, K. (2002). Rehabilitation of swallowing by exercise in tube-fed patients with pharyngeal dysphagia secondary to abnormal UES opening. *Gastroenterology*, 122(5), 1314-1321.

Shiley, S. G., Hargunani, C. A., Skoner, J. M., Holland, J. M., & Wax, M. K. (2006). Swallowing function after chemoradiation for advanced stage oropharyngeal cancer. *Otolaryngology--Head and Neck Surgery*, 134(3), 455-459.

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

Sluijs, E. M., Kok, G. J., & Zee, J. v. d. (1993). Correlates of exercise compliance in physical therapy. *Physical Therapy*, 73(11), 771-782. Retrieved from

<http://ptjournal.apta.org/content/73/11/771.full.pdf+html?frame=sidebar>

Smith, R. V., Kotz, T., Beitler, J. J., & Wadler, S. (2000). Long-term swallowing problems after organ preservation therapy with concomitant radiation therapy and intravenous hydroxyurea: Initial results. *Archives of Otolaryngology--Head & Neck Surgery*, 126(3), 384-389.

Stoeckli, S., Huisman, T., Seifert, B., & Martin-Harris, B. J. W. (2003). Interrater reliability of videofluoroscopic swallow evaluation. *Dysphagia*, 18(1), 53-57. doi:10.1007/s00455-002-0085-0

Stubblefield, M. D. (2011). Radiation fibrosis syndrome: Neuromuscular and musculoskeletal complications in cancer survivors. *Clinical Review*, 3(11), 1041-1054.

Sudhoff, H. H., Schwarze, H. P., Winder, D., Steinstraesser, L., Gerner, M., Stanley, M., & Goon, P. K. (2011). Evidence for a causal association for HPV in head and neck cancers. *European Archives of Otorhinolaryngology*, 268(11), 1541-1547.

Tang, Y., Shen, Q., Wang, Y., Lu, K., Wang, Y., & Peng, Y. (2011). A randomized prospective study of rehabilitation therapy in the treatment of radiation-induced dysphagia and trismus. *Strahlentherapie Und Onkologie*, 187(1), 39-44.

van der Molen, L., van Rossum, M. A., Burkhead, L. M., Smeele, L. E., Rasch, C. R. N., & Hilgers, F. J. M. (2011). A randomized preventive rehabilitation trial in advanced head and

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

neck cancer patients treated with chemoradiotherapy: Feasibility, compliance, and short-term effects. *Dysphagia*, 26, 155-170. doi:10.1007/s00455-010-9288-y

Veis, S., Logemann, J., & Colangelo, L. (2000). Effects of three techniques on maximum posterior movement of the tongue base. *Dysphagia*, 15(3), 142-145.

Virani, A., Kunduk, M., Fink, D. S., & McWhorter, A. J. (2015). Effects of 2 different swallowing exercise regimens during organ-preservation therapies for head and neck cancers on swallowing function. *Head & Neck*, 37(2), 162-170. doi:10.1002/hed.23570

Vissink, A., Jansma, J., Spijkervet, F. K. L., Burlage, F. R., & Coppes, R. P. (2003). Oral sequelae of head and neck radiotherapy. *Critical Reviews in Oral Biology and Medicine*, 14(3), 199-212.

Webster, K., Cella, D., & Yost, K. (2003). The functional assessment of chronic illness therapy (FACIT) measurement system: Properties, applications, and interpretation. *Health and Quality of Life Outcomes*, 1(1), 79. doi:10.1186/1477-7525-1-79

Wilcox, F., Liss, J. M., & Siegel, G. M. (1996). Interjudge agreement in videofluoroscopic studies of swallowing. *Journal of Speech and Hearing Research*, 39(1), 144-152.

Wilson, G., Bentzen, S. M., & Harari, P. M. (2006). Biologic basis for combining drugs with radiation. *Seminars in Radiation Oncology*, 16(1), 9. doi:10.1016/j.semradonc.2005.08.001

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

Wilson, J. A., Carding, P. N., & Patterson, J. M. (2011). Dysphagia after nonsurgical head and neck cancer treatment: Patients' perspectives. *Otolaryngology - Head and Neck Surgery*, 145(5), 767-771.

World Health Organization. (2013). *How to use the ICF: A practical manual for using the international classification of functioning, disability and health (ICF)*. Geneva: WHO:

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Appendices

Appendix A

Permission to be Contacted Form

Return this form to:

Attn: Laurie Slovarp
CSD Department
Fax: 406-243-2362

Study Title:

Preventative Dysphagia Intervention for Patients with Head and Neck Cancer receiving Chemoradiation Therapy (CRT)

Investigator(s):

Laurie Slovarp M. S., SLP-CCC, BRS-S, The University of Montana, Department of
Communicative Sciences and Disorders (CSD 031), (406)243-2107

Purpose

You are being asked to be contacted by researchers at the University of Montana, to learn more about taking part in a research study comparing two different exercise programs used to help prevent or minimize dysphagia (an impairment in the ability to swallow). This study is designed to help develop an optimal treatment protocol that minimizes the prevalence and degree of dysphagia in patients treated with chemoradiation therapy (CRT) for oral, pharyngeal, and/or laryngeal cancer, while also minimizing discomfort.

Statement of consent to be contacted by the researchers:

I, _____, agree to be contacted by the researchers at The University of
Montana

(printed name)

for additional information on the above mentioned study. I am in no way agreeing at this time to participate in the study.

You may contact me via:

☐ Phone: _____

☐ Email: _____

Patient Signature

Date

Patient's projected start date of radiation therapy: _____

Appendix B

NUTRITIONAL AND PAIN QUESTIONNAIRE

Participant code: _____ Date: _____

Current Weight: _____

Tube Feeding Use:

Do you currently have a tube inserted into your stomach for nutrition? Mark the correct answer

☐ Yes

☐ No

If yes, please answer the following question.

If no, please skip to pain rating section.

Approximately, what percentage of your daily food intake is consumed using your tube?

Check one option:

☐ 0-10%

☐ 10-25%

☐ 25-50%

☐ 50-75%

☐ 75-90%

☐ 90-100%

Swallowing Pain Rating:

Please use the following scale to indicate the amount of pain you have with swallowing.

☐ 0 (no pain)

☐ 1-2 (mild discomfort)

☐ 3-4 (moderate discomfort)

☐ 5-6 (severe pain)

☐ 7-8 (very severe pain)

☐ 9-10 (excruciating pain)

Functional Oral Intake Scale (FOIS): Please circle the diet level that best describes your nutritional intake.

Category	Level	Description
Non-Oral	1	Nothing by mouth (NPO)
	2	Tube dependent with minimal attempts of food or liquid
	3	Tube dependent with consistent intake of liquid or food
	4	Total oral diet of a single consistency (e.g., all pureed foods)
Full-Oral	5	Total oral diet with multiple consistencies but requiring special preparation or swallowing compensatory strategies
	6	Total oral diet with multiple consistencies without special preparation, but with specific food limitations (e.g., avoiding dry foods)
	7	Total oral diet with no restriction (eat anything you would like)

Appendix C

The M.D. Anderson Dysphagia Inventory

Participant code: _____ Date: _____

Week post-CRT start: _____ Weeks/months post-CRT end: _____

Please read each statement and circle the response which best reflects your experience in the past week.

1. My swallowing ability limits my day-to-day activities.
☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree
2. (E2) I am embarrassed by my eating habits.
☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree
3. (F1) People have difficulty cooking for me.
☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree
4. (P2) Swallowing is more difficult at the end of the day.
☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree
5. (E7) I do not feel self-conscious when I eat.
☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree
6. (E4) I am upset by my swallowing problem.
☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree
7. (P6) Swallowing takes great effort.
☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree
8. (E5) I do not go out because of my swallowing problem.
☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree
9. (F5) My swallowing difficulty has caused me to lose income.
☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree
10. (P7) It takes me longer to eat because of my swallowing problem.
☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree
11. (P3) People ask me, "Why can't you eat that?"
☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree
12. (E3) Other people are irritated by my eating problem.
☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree

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13. (P8) I cough when I try to drink liquids.

☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree

14. (F3) My swallowing problems limit my social and personal life.

☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree

15. (F2) I feel free to go out to eat with my friends, neighbors, and relatives.

☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree

16. (P5) I limit my food intake because of my swallowing difficulty.

☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree

17. (P1) I cannot maintain my weight because of my swallowing problem.

☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree

18. (E6) I have low self-esteem because of my swallowing problem.

☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree

19. (P4) I feel that I am swallowing a huge amount of food.

☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree

20. (F4) I feel excluded because of my eating habits.

☐ Strongly Agree ☐ Agree ☐ No Opinion ☐ Disagree ☐ Strongly Disagree

Appendix D

Eating Assessment Tool (EAT – 20)

Participant code: _____

Date: _____

Circle the appropriate response:

To what extent are the following scenarios problematic for you?	0 = No problem 5 = Severe problem					
	0	1	2	3	4	5
1. My swallowing problem has caused me to lose weight.	0	1	2	3	4	5
2. My swallowing problem interferes with my ability to go out for meals.	0	1	2	3	4	5
3. My swallowing problem interferes with my work or other activities.	0	1	2	3	4	5
4. Swallowing liquids takes extra effort.	0	1	2	3	4	5
5. Swallowing solids takes extra effort.	0	1	2	3	4	5
6. Swallowing pills takes extra effort	0	1	2	3	4	5
7. I have altered my diet because of my swallowing problem.	0	1	2	3	4	5
8. Swallowing is painful.	0	1	2	3	4	5
9. The pleasure of eating is affected by my swallowing.	0	1	2	3	4	5
10. When I swallow food sticks in my throat.	0	1	2	3	4	5
11. When I swallow food sticks in my chest.	0	1	2	3	4	5
12. I cough when I eat.	0	1	2	3	4	5
13. I am afraid to eat because of my swallowing problem.	0	1	2	3	4	5
14. My swallowing problem is a burden to my family.	0	1	2	3	4	5
15. I get tired when I eat.	0	1	2	3	4	5
16. I avoid eating in front of people.	0	1	2	3	4	5
17. I am afraid of choking in my sleep.	0	1	2	3	4	5
18. I become short of breath when I eat.	0	1	2	3	4	5
19. People perceive me as sick because of my swallowing problem.	0	1	2	3	4	5
20. Swallowing is stressful.	0	1	2	3	4	5

TOTAL

Appendix E

SUBJECT INFORMATION AND INFORMED CONSENT

Study Title:

Prophylactic Dysphagia Intervention for Patients with Head and Neck Cancer receiving Chemoradiation Therapy (CRT)

Investigator(s):

Laurie Slovarp M.S., SLP-CCC, BRS-S, The University of Montana, Department of Communicative Sciences and Disorders (CSD 031), (406)243-2107

Amy Glatt B. A., Research Assistant. The University of Montana, Department of Communicative Sciences and Disorders (CSD), (406)243-2107

Special instructions

This consent form may contain words that are new to you. If you read any words that are unclear to you, please ask the person who gave you this form to explain them to you.

Purpose

You are being asked to take part in a research study comparing two different exercise programs used to help prevent or minimize difficulty swallowing (called “dysphagia”). This study is designed to help develop a way to minimize the degree and discomfort of dysphagia in patients treated with chemoradiation therapy (CRT) for oral, pharyngeal, and/or laryngeal cancer.

Procedures

If you agree to take part in this research study you will be asked to

1. undergo a baseline instrumental swallow study (modified barium swallow (MBS) or fiberoptic endoscopic evaluation of swallowing (FEES)),
2. complete daily swallowing exercises throughout your radiation therapy, and
3. periodically fill out a number of brief questionnaires to assess your swallowing function.

You will be assigned to one of two treatment groups. Both treatment groups will be given a series of swallowing exercises. Both types of exercise have been shown to be helpful for minimizing dysphagia during and after CRT.

Swallowing exercise group: The exercises for this group will primarily emphasize swallow strengthening with primarily exercises that require you to swallow (see “*Swallowing Exercises Handout*”).

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Non-swallowing exercise group: The exercises for this group will not require swallowing during the exercises; rather the exercises will focus primarily on flexibility of the muscles used during swallowing (see “*Non-Swallowing Exercises Handout*”).

The following is a description of the timeline/phases of the study.

- **Baseline Instrumental Swallow Study:** Prior to beginning chemoradiation, you will undergo an instrumental swallow examination (either a Modified Barium Study (MBS) or a Fiberoptic Endoscopic Evaluation of Swallowing (FEES), either of which are routinely recommended prior to beginning chemoradiation to the mouth, pharynx, or larynx)
- **Training Phase:** You will be seen by the investigator(s) for 2-3 sessions for an initial interview and for training to learn how to perform your exercise program and how to track compliance to the program. A paper tracking form will be provided and you will be asked to keep a daily record of your exercises.
- **Treatment Phase:** Following the training phase, you will be seen once every two weeks throughout CRT (or more if necessary given the severity of your dysphagia) to document progress using a number of tools. You will fill out three questionnaires that will provide the following information. 1) The amount of food you take via a feeding tube versus eating by mouth, 2) the amount of pain you are experiencing, and 3) behaviors, responses and quality of life related to swallowing.
- **Post-treatment Phase:** After CRT, the investigators will see you as appropriate for dysphagia therapy until you return to full per oral (P.O., by mouth) intake with the least restrictive diet possible. Your dysphagia therapy at that point will be guided by the nature of your dysphagia and best practices. You will be followed during this phase for three months. If you do not need active dysphagia therapy during the entire three month period, you will be asked to fill out the data questionnaires via phone or mail once per month.
- **Long-term Phase:** After you have been discharged from therapy, the principal investigator (Laurie Slovarp) will follow up with you at six months post-treatment (three months following the post-treatment phase) and 12 months post-treatment. From that point on data collection will take place once per year for 10 years using the same data questionnaires used during the treatment and post-treatment phases. A self-addressed, stamped envelope will be included for you to return them at no cost to you. This should take you no more than 10 minutes.

Risks/Discomforts

You may experience pain, fatigue, frustration or aspiration (small amounts of food or liquid into your airway) during the therapy. The therapies chosen are considered safe and ethical practice and will not exceed the expected risks/discomforts from traditional dysphagia therapy. You will be able to take short breaks during treatment to help alleviate any pain, fatigue, or frustration that may occur as a result of therapy. You also may drop out of the study at any time without any penalty or effect on your medical treatment or care. The researchers will communicate with your medical team and will report any concerning effects that may warrant medical management, although it is highly unlikely that participation in this study will lead to any such effects.

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Benefits

There is no guarantee that you will receive any direct benefit from taking part in this study, but participation may minimize your swallowing impairment severity while and after you complete CRT. Specifically, the exercises chosen for the study have been shown to improve swallowing function following CRT (Carrol, Locher, Canon, Bohannon, McColloch, & Magnuson, 2008; Hutcheson & Lewin, 2012; Vander Molen, Van Rossum, Burkhead, Smeele, Coen, & Hilgers, 2011). You will also receive swallowing therapy from a certified Speech Language Pathologist. Additionally, you will be contributing to the knowledge base on how best to treat patients with head and neck cancer who suffer from dysphagia.

Payment

There will be no cost to you for participating in this study and you will not receive payment for participating. However, costs that are related to the standard treatment for your dysphagia and not related to this research will be billed to you or your insurance company (i.e., modified barium swallow studies and swallowing therapy following completion of CRT). If it is necessary for you to have additional swallowing therapy following completion of CRT, and you are unable to pay for such therapy (e.g., uninsured or underinsured), you will have the option to receive therapy at no charge through the RiteCare Speech, Language, and Hearing Clinic at The University of Montana.

Confidentiality

Your identity and the information that is obtained about you during this study will remain confidential to the extent provided by law. However, the study investigator, National Institute of Health, The US Food and Drug Administration (FDA), study staff, study sponsor, and the Joint Investigational Review Board may review your records to verify study related information. If the study results are published or presented, you will not be identified by your name.

Prior to the first screening, you will be given this research consent form, and HIPAA (Health Insurance Portability and Accountability Act) form. These will be the only forms containing your personal information (name, date of birth, address, phone number, email). The consent form has a place to write in a non-identifiable participant code. Your identification on all subsequent documents (other than the consent form and the HIPAA form) specifically pertaining to the research will be by the non-identifiable code rather than your name and will be kept in a locked file cabinet in room 031 in the Department of Communicative Sciences and Disorders. Consent and HIPAA forms, as well as medical records pertaining to standard dysphagia care that is outside the scope of the specific research protocol, will be kept in your therapy chart, which will be kept in a locked file cabinet. This will ensure that coded data is not easily associated with your name. Only the research team and necessary medical professionals outlined by the laws of HIPAA will have access to these files. All data files will be identified with the same anonymous code and will be password protected.

Compensation for Injury

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

Although we do not foresee any risk in taking part in this study, the following liability statement is required in all University of Montana consent forms: “In the event that you are injured as a result of this research you should individually seek appropriate medical treatment. If the injury is caused by the negligence of The University or any of its employees, you may be entitled to reimbursement or compensation pursuant to the Comprehensive State Insurance Plan established by the Department of Administration under the authority of M.C.A., Title 2, Ch 9. In the event of a claim for such injury, further information may be obtained from The University’s Claims representative or University Legal Counsel.” (Reviewed by University Legal Counsel, July 6, 1993)

It is not the regular policy of The University of Montana or Saint Patrick Hospital, the sponsor of this research study, to provide compensation for injury beyond what is stated in the above paragraph. You still have all of your legal rights to seek other compensation.

Pregnancy/Contraception

You should not undergo a modified barium swallow (MBS) study if you are pregnant. If you are pregnant, or become pregnant during the study, be sure to inform us. If this does happen, you will be given the option to have endoscopic swallow study (FEES) study instead. Your participation in this study poses no other risks pertaining to pregnancy or contraception

Voluntary Participation/Withdrawal

Your decision to take part in this research study is voluntary. You may refuse to take part in or you may withdraw from the study at any time without penalty or loss of benefits to which you are normally entitled. If you decide to withdraw, contact the lead investigator, Laurie Slovarp MS, SLP-CCC, BRS-S at The University of Montana, Department of Communicative Sciences and Disorders (CSD 031), (406)243-2107.

Questions

This research study has been reviewed by the Joint Investigational Review Board (JIRB) for the purpose of protecting your safety and rights. The JIRB was instituted under Federal and State law to review studies such as this one in order to protect research participants from:

- unnecessary risks
- risks that outweigh the benefits
- procedures that are scientifically unnecessary

If you have any questions regarding your rights as a research study participant, you may call the Joint Investigational Review Board (JIRB) Coordinator at (406) 329-5669.

If you have any questions about the research procedures now or during the study contact: Laurie Slovarp, The University of Montana, Department of Communicative Sciences and Disorders (CSD 031), (406)243-2107.

Video Recordings

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

We would like to videotape the study procedures. Videotaping is completely voluntary. Participants are free to withdraw their recordings from this study at any time without penalty and without jeopardizing future services at The University of Montana or Providence Saint Patrick Hospital. We will provide an opportunity for you to review and edit the recordings if you request. We may also want to use the recordings for future related research or for educational purposes. Although the recordings will not be labeled with your name, someone who knows you may be able to identify you from the recordings.

We would like your consent to the following specific uses of the video recordings made of you. If you have any questions or concerns about the recordings or their use, you are free to restrict the uses described below. Restrictions will not affect your participation in any current or future research studies or clinical services at the RiteCare Speech, Language and Hearing Clinic or at Saint Patrick Hospital.

Do you consent to being video recorded for Research Purposes? (i.e., viewing/listening by The University of Montana faculty, students, and staff for research purposes)

☐ Yes ☐ No initials: _____

Do you consent to being video recorded for the following educational Purposes?

- Viewing/listening by The University of Montana faculty, students, and staff for education (e.g., course presentations, lectures, assignments, etc.)
☐ Yes ☐ No initials: _____
- Viewing/listening by participants in any educational activities at the discretion of Speech Pathology and Audiology faculty and staff. The educational activities include conferences and workshops attended by students, professionals, and caregivers. The recordings may be shared through any medium, provided it is not available to the general public.
☐ Yes ☐ No initials: _____
- Viewing/listening by the general public at activities or through media sponsored or licensed by The University of Montana, or its faculty or staff (e.g., Internet/World Wide Web, local television)? ☐ Yes ☐ No initials: _____
- Viewing/listening by the general public through licensed commercial enterprises for educational or research purposes, for example a CD-ROM enclosed in a textbook.
☐ Yes ☐ No initials: _____

Decline of Video/Audio Recording

- If you would not like to be video or audio recorded, place your initials here _____.

STATEMENT OF CONSENT

If you agree to be a participant of this study, sign one of the following two consent statements:

Statement of Consent to participate as a treatment participant

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

I have read the above description of this research study. I have been informed of the risks and benefits involved, and all my questions have been answered to my satisfaction. Furthermore, I have been assured that any future questions I may have will also be answered by a member of the research team. I voluntarily agree to take part in this study. I understand I will receive a copy of this consent form.

By signing this consent form, I have not waived any of the legal rights which I otherwise would have as a participant in a research study.

I voluntarily agree to participate in this study and authorize the use and disclosure of my private health information as outlined in this form.

Participant Code: _____

Participant Name (printed): _____ Date of birth: _____

Age: _____ Gender: ☐ male ☐ female

Address: _____

Primary phone number: _____ Alternative phone: _____

Email address: _____ Radiation Oncologist: _____

We may need to contact you regarding scheduling. How may we contact you?

☐ Telephone ☐ Text messaging ☐ email

Participant signature: _____ Date: _____

Investigator Signature: _____

Consent to participate only as a non-treatment control participant

I decline to participate in the baseline, training and treatment phases of this study, but agree to participate as a non-treatment control participant. I agree to answer the questionnaires at the same frequencies as the treatment participants.

Participant Code: _____

Participant Name (printed): _____ Date of birth: _____

Age: _____ Gender: ☐ male ☐ female

Address: _____

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

Primary phone number: _____ Alternative phone: _____

email address: _____ Radiation Oncologist: _____

How may we contact you?

☐ Telephone ☐ Text messaging ☐ email

Participant signature: _____ Date: _____

Investigator Signature: _____

Appendix F

Prophylactic Dysphagia Intervention for Patients with Head and Neck Cancer Receiving Chemoradation Therapy (CRT)

Authorization for Access to Personal Health Information

A federal government rule has been issued to protect the privacy rights of patients. The rule is designed to protect the confidentiality of your personal health information. We are required by these new regulations to obtain your authorization to share personal health information that may reveal your identity.

What Information will be Used or Disclosed

For this research study, the health information to be used or disclosed includes information contained in your existing medical records and new information created or collected during this study. Your records may include information about your physical examinations, medical procedures (e.g., surgeries, swallow studies, chemoradiation), medical history, and any other data collected or reviewed during the course of the study as described in the consent form.

Purpose for Use or Disclosure

The purpose for use or disclosure of information gathered will be to measure the effectiveness of the therapies being studied in this research and to develop a better understanding of how best to treat dysphagia in patients with head and neck cancer.

Who May Use or Disclose Information

The persons and organizations that may use or disclose your individually identifiable health information may include: your physicians, the study investigator (Laurie Slovarp) and investigator staff.

Who May Receive Information

The persons and entities that may receive your personal health information may include: National Institute of Health, The US Food and Drug Administration (FDA), and the Saint Patrick Hospital/Community Medical Center Joint Investigational Review Board.

Every effort will be made to maintain confidentiality of information accessed. However, absolute confidentiality cannot be guaranteed. Once your personal health information is released it may be re-disclosed, at which point your health information will no longer be protected by federal privacy regulations.

Duration of Authorization

This authorization does not have an expiration date. If you do not cancel this authorization, then it will remain in effect indefinitely.

Right to Refuse, Withdraw or Cancel Authorization

You may refuse to sign this authorization. If you refuse to sign this authorization, you will not be able to take part in this study. However, you will not be penalized or lose any benefits to which you are otherwise entitled. You will continue to receive treatment for your condition.

You have the right to cancel this authorization or withdraw from this study at any time with no penalty. If you choose to do so, you must notify the study investigator in writing at Laurie Slovarp, Department of Communicative Sciences and Disorders, The University of Montana, 32 Campus Dr., Missoula, MT 59812. Data collected prior to cancellation of this authorization may be used in order to preserve the scientific integrity of the study.

Patient Access to Records

You have the right to access your medical records at any time. However, you will not be able to access study specific information until the study is completed, at which time your right of access will be restored.

TWO PROPHYLACTIC-DYSPHAGIA INTERVENTIONS FOR HNC

Privacy Authorization

I have read this Privacy Authorization and have had my questions answered to my satisfaction at this time. I understand that by signing this consent, I authorize the release of my medical records and health information related to this study. I authorize the use, disclosure, review, duplication, storage and data transfer of my medical records and study information. I understand this information may be obtained by the persons and organizations stated above. I will receive a copy of this signed authorization.

I authorize the following medical personnel/healthcare facilities to release my records.

_____	_____	_____
Name of Physician/Healthcare Facility	Telephone	Fax

_____	_____	_____	_____
Street Address	City,	State,	Zip Code

_____	_____	_____
Name of Physician/Healthcare Facility	Telephone	Fax

_____	_____	_____	_____
Street Address	City,	State,	Zip Code

_____	_____	_____
Name of Physician/Healthcare Facility	Telephone	Fax

_____	_____	_____	_____
Street Address	City,	State,	Zip Code

_____	_____	_____
Signature of Participant	Date	Name of Participant (Printed)

Or

_____	_____	_____
Signature of Legal Representative	Date	Name of Legal Representative (Printed)

Relationship to Participant

Appendix G

Swallowing Exercise Instructions C-PSE Group

Mendelsohn

When you swallow your throat elevates and then immediately drops back down. To do this, swallow and hold your throat up 2-3 seconds. To do this you will hold the contraction of the swallowing muscles. You have already swallowed so the food is gone, you are just not releasing the swallow. You will not be able to breathe while you are holding your throat up. **Do this exercise 15 times in a row, 3 times per day, 7 days per week.**

Effortful Swallow

When you swallow squeeze all your swallowing muscles as hard as you can. You can do this while swallowing anything. **Do this exercise 20 times in a row, 3 times per day, 7 days per week.**

Masako

Do this exercise when you only have saliva in your mouth. Place your tongue between your teeth and lightly bite down with enough force to hold your tongue in place. Be sure to keep your tongue between your teeth and swallow. **Do this exercise 10 times in a row, 3 times per day, 7 days per week.**

Shaker

This exercise has two parts. Both parts requires the same type of motion. Lie flat on your back without a pillow and lift your head so that your chin approaches your chest. Do not lift your shoulders off of the ground. Try to look at your toes. Part 1: hold your head up for one minute (or as long as you can). Part 2: lift and lower your head 20 times holding at the top each time for just 1-2 seconds. **Do this exercise three times per day, 7 days per week.**

Appendix H

Swallowing Exercise Instructions ID-PSE group

Shaker

This exercise has two parts. Both parts requires the same type of motion. Lie flat on your back without a pillow and lift your head so that your chin approaches your chest. Do not lift your shoulders off of the ground. Try to look at your toes. Part 1: hold your head up for one minute (or as long as you can). Part 2: lift and lower your head 20 times holding at the top each time for just 1-2 seconds. **Do this exercise three times per day, 7 days per week.**

Falsetto “ee”

Take a deep breath and then say a soft, high pitched “ee” sound as long as you can. **Do this exercise 6 times in a row, 3 times per day, 7 days per week.**

Tongue-Base Retraction

Stick your tongue out and grab it between your fingers with a washcloth. Then pull your tongue back into your mouth as far as you can, providing resistance by holding your tongue with the washcloth. You will likely have to stop to swallow intermittently. If you have trouble holding your tongue, you can just stick your tongue out and pull it in your mouth without resistance. If you do it this way, do it in front of a mirror and try to not curl your tongue tip. You should feel the back of your tongue touch the back of your throat. If it makes you gag, you likely did it correctly. **Do this exercise 10 times, 3 times per day, 7 days per week.**

Lingual Range of Motion Exercises

Stick out your tongue and move it up towards your nose and then down towards your chin. Stretch as far as you can in both directions. **Repeat 10 times, 3 times per day, 7 days per week.**

Move your tongue in a circle on the outside of all of your teeth (as if you are cleaning food off of the outer surface of your teeth). **Repeat 10 times, 3 times per day, 7 days per week.**

Press your tongue in to each of your cheeks (going back and forth). Stretch as far as you can.

Do this exercise 10 times, 3 times per day, 7 days per week.

Jaw Range of Motion Exercises

Open your mouth as far as you can and hold for 2-3 seconds, close and repeat. **Do this exercise 10 times, 3 times per day, 7 days per week.**

Move your jaw from side to side as far as you can each way. **Do this exercise 10 times, 3 times per day, 7 days per week.**

Appendix I

Swallowing Exercise Tracking Sheet

Instructions: List the number of repetitions and sets of each exercises you performed each day. If you did not complete a set of exercises please list which exercise it was and why you could not perform it.

Participant Number:					
Exercises (S)	Mendelsohn	Effortful Swallow	Masako	Shaker	Comments:
Date:					
Date:					
Date:					
Date:					
Date:					
Date:					
Date:					
Date:					
Date:					
Date:					
Date:					
Date:					
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Date:					
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Date:					
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Date:					

Appendix J

Swallowing Exercise Tracking Sheet

Instructions: List the number of repetitions and sets of each exercises you performed each day. If you did not complete a set of exercises please list which exercise it was and why you could not perform it.

Participant Number:						
Exercises (NS)	Shaker	Falsetto “ee”	Tongue- Base Retraction	Tongue Range of Motion	Jaw Range of Motion	Comments:
Date:						
Date:						
Date:						
Date:						
Date:						
Date:						
Date:						
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